RADICAL CHEMISTRY OF NEW CYCLIC AND ACYCLIC AZO COMPOUNDS

麥馬斯達大學

新偶氮化合物的游離基化學

楊信炯

一九七七年八月

TO

MY PARENTS

AND

MY WIFE, KITTY

RADICAL CHEMISTRY OF α-AZODIPHENYLCARBINOLS AND OF 2-ACETOXY-2-METHYL-5,5-DIALKYL-Δ^3-1,3,4-OXADIAZOLINES

By

DOMINIC WAI KWING YEUNG, B.Sc.

A Thesis
Submitted to the Faculty of Graduate Studies
in Partial Fulfilment of the Requirements
for the Degree
Doctor of Philosophy

McMaster University
August 1977

© DOMINIC WAI KWING YEUNG 1978

DOCTOR OF PHILOSOPHY
(Chemistry)

McMASTER UNIVERSITY
Hamilton, Ontario

TITLE: Radical Chemistry of α-Azodiphenylcarbinols and of 2-Acetoxy-2-Methyl-5,5-Dialkyl-Δ^3-1,3,4-Oxadiazolines

AUTHOR: Dominic Wai Kwing Yeung, B.Sc. (Hong Kong University)

SUPERVISOR: Professor John Warkentin

NUMBER OF PAGES: xii, 190

ABSTRACT

A series of new α-azodiphenylcarbinols was synthesized by mild deacetylation (with methyl lithium) of the corresponding azoacetates which, in turn, were prepared by reactions of either lead tetraacetate or bromine with benzophenone monosubstituted hydrazones. The chemistry of these new types of α-azocarbinols was studied in several aspects. Firstly, the kinetics of thermolysis of these compounds in carbon tetrachloride and in benzene solutions are reported, and the mechanism of the decomposition (radical chain, induced) is discussed. The effects of inhibitors on the decomposition is also examined. Secondly, the potential synthetic applicability of these compounds is illustrated by the hydroalkylation of several unsaturated compounds. Thirdly, the catalytic role of phenol in the radical chain reactions is discussed qualitatively. Fourthly, the e.s.r. spectra of nitroxides, resulting from the reactions of these compounds with nitrosobenzene, were obtained at room temperature in degassed benzene solutions. The a_N and g values of these nitroxides are reported.

Another part of the thesis describes the synthesis and chemistry of two new 2-acetoxy-2-methyl-5,5-disubstituted-Δ^3-1,3,4-oxadiazolines. The thermolysis of these oxadiazolines was investigated, both in nitrobenzene and in benzene solutions. The results of kinetics are presented, and a probable mechanism of the decomposition, through diazenyl radical intermediates, is examined.

Radical intermediates are involved in the chemistry of these new azo compounds. α-Azocarbinols decompose by a radical-induced chain mechanism and their synthetic application involves chain addition. The oxadiazolines undergo unimolecular, homolytic cleavage. A review of radical chemistry, presented in Chapter I, is therefore appropriate.

ACKNOWLEDGEMENTS

I am much indebted to Professor John Warkentin for his guidance, encouragement, advice, enthusiasm and helpful discussions throughout the course of this work. It is also my pleasure to thank all the people in the Department of Chemistry for their assistance and cooperation during these studies, especially to the technical staff in obtaining 100 MHz p.m.r., ^{13}C.m.r., e.s.r. as well as mass spectra. Finally, I wish to express my gratitude to McMaster University for financial support as well as for providing sufficient research facilities to carry out the present work.

TABLE OF CONTENTS

	Page
Abstract	ii
Acknowledgements	iv
CHAPTER 1 FREE RADICAL CHEMISTRY	1
1.1 Introduction	1
1.2 Production of Radicals	2
1.2.1 Thermal Homolysis	2
1.2.2 Irradiation	7
1.2.3 Redox Reactions	7
1.3 Detection of Free Radicals by the Spin-Trap Technique	8
1.4 Classification of Radical Reactions	11
1.4.1 Unimolecular Reactions	11
1.4.1.a Radical Fragmentations	11
1.4.1.b Radical Rearrangements	12
1.4.1.c Radical Cyclizations	13
1.4.2 Bimolecular Reactions between Two Radicals	14
1.4.2.a Combinations	14
1.4.2.b Disproportionations	15
1.4.3 Bimolecular Reactions between Radicals and Molecules	16
1.4.3.a Substitutions	16
1.4.3.b Abstractions	17
1.4.3.c Additions	18
1.4.4 Electron-Transfer Reactions of Radicals	27
1.5 Some General Characteristics of Radical Chain Reactions	27

Page

1.6 Factors Governing Radical Reactions 29
    1.6.1 Stabilization 30
    1.6.2 Polar Effects 30
    1.6.3 Steric Effects 31
    1.6.4 Solvent Effects 31
1.7 Kinetic Aspects of Free-Radical Chain Reactions 32
1.8 Bond Dissociation Energies 36
1.9 Catalysis in Free-Radical Chain Reactions 37

CHAPTER 2 REACTIONS OF LEAD TETRAACETATE WITH KETONE HYDRAZONES 41
2.1 Unsubstituted Hydrazones 41
2.2 N-Monosubstituted Hydrazones 42
2.3 N,N-Disubstituted Hydrazones 45

CHAPTER 3 α-AZOCARBINOLS 46

CHAPTER 4 DECOMPOSITION OF Δ^3-1,3,4-OXADIAZOLINES 56

CHAPTER 5 RESULTS AND DISCUSSION 64
5.1 Synthesis of α-Azodiphenylcarbinols 64
5.2 Chemistry of α-Azodiphenylcarbinols 75
    5.2.1 Thermal Decomposition 75
        5.2.1.a Decomposition in Carbon Tetrachloride 75
        5.2.1.b Decomposition in Benzene 81
    5.2.2 Reactions with Olefins and Azobenzene 84
    5.2.3 Reactions with Olefins in the Presence of Phenol 90

Page

5.2.4 Reactions with Nitrosobenzene in Benzene Solutions 119

5.3 Synthesis and Pyrolysis of 2-Acetoxy-2-Methyl-5,5-Dialkyl-Δ^3-1,3,4-Oxadiazolines 120

5.3.1 Synthesis 120

5.3.2 Structures 125

5.3.3 Mechanism of Oxidative Cyclization 127

5.3.4 Pyrolysis of Oxadiazolines 127

5.3.5 Kinetics of Thermolysis 132

5.3.6 Mechanism of Decomposition 135

CHAPTER 6 EXPERIMENTAL 142

6.1 General 142

6.2 Preparation of Benzophenone Hydrazone 143

6.3 Preparation of Diphenyldiazomethane 143

6.4 Preparation of Grignard Reagents 144

6.5 Preparation of Benzophenone Substituted Hydrazones (ϕ_2C-NNHR) 145

6.5.1 Preparation of benzophenone tert-butylhydrazone 145

6.5.2 Preparation of benzophenone-(methyl- or 2-hydroxyethyl-)hydrazone 146

6.5.3 Preparation of benzophenone isopropyl-(benzyl-, ethyl-, cyclohexyl- or allyl-)hydrazone 147

6.6 Preparation of Lead Tetraacetate (LTA) 147

6.7 Preparation of Alkylazodiphenylmethylacetates 148

6.7.1 With LTA Oxidation 148

Page

6.7.2 Oxidation with bromine 148
6.8 Preparation of α-Azodiphenylcarbinols 149
6.9 Chemistry of α-Azodiphenylcarbinols 150
6.9.1 Thermolysis 150
6.9.2 Kinetics of Decomposition of tert-butylazodiphenylcarbinol 150
6.9.3 Effects of thiophenol, phenol and triphenylstannane on the decomposition 153
6.9.4 Spin trapping by nitrosobenzene 154
6.9.5 Trapping with unsaturated compounds 154
6.9.6 Reactions of methylazodiphenylcarbinol with norbornene in the presence of D_2O 155
6.9.7 Reactions of olefins in the presence of phenol 156
6.10 Independent Synthesis of Tert-butyl-1,2-diphenylhydrazine and Methyl-1,2-diphenylhydrazine 163
6.11 Thermolysis of Tert-butylazodiphenylmethyl Acetate 163
6.12 Preparation of Ketone Acetylhydrazones 164
6.13 Preparation of Acetone-d_6 Acetylhydrazone 165
6.14 Preparation of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines 165
6.15 Preparation of 2-Acetoxy-2-methyl-5,5-bis(trideuteromethyl)-Δ^3-1,3,4-oxadiazolines 166
6.16 Chemistry of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines 166

Page

6.16.1 Thermolysis 166

6.16.2 Kinetics of thermolysis 167

6.16.3 Attempts to trap intermediates in pyrolysis of 2-acetoxy-2-methyl-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline 167

6.17 Reactions of 1-Acetoxyethyl-2-propenyl Ether ($CH_3\overset{O}{\overset{\|}{C}}OCH(CH_3)OC(CH_3)=CH_2$) with Bromine 168

6.18 Preparation of 3-Methyl-2-buten-2-ol Acetate 168

6.19 Preparation of 2-Acetoxy-2,3-epoxy-3-methylbutane 169

6.20 Thermolysis of 2-Acetoxy-2,3-epoxy-3-methylbutane in Benzene and in Carbon Tetrachloride Solutions 170

CHAPTER 7 SUMMARY 171

REFERENCES 173

APPENDIX I COMPUTER PROGRAM FOR EVALUATING FIRST-ORDER RATE CONSTANTS 189

LIST OF TABLES

Page

Table 1 Benzophenone N-Monosubstituted Hydrazones 66

Table 2 Yields and Properties of Azoacetates 71

Table 3 Properties of α-Azodiphenylcarbinols 73

Table 4 Kinetics of Decomposition of tert-Butylazodiphenylcarbinol at 35° 79

Table 5 Hydro-tert-butylation of Unsaturated Compounds 85

Table 6 Hydro-isopropylation of Unsaturated Compounds 86

Table 7 Hydroethylation of Unsaturated Compounds 87

Table 8 Hydromethylation of Unsaturation Compounds 88

Table 9 Yields and Properties of Substituted 1,2-Diphenylhydrazines 89

Table 10 The Splitting Constants (gauss) of Nitroxide Radicals 111

Table 11 The Splitting Constants (gauss) of Some Known Nitroxides 112

Table 12 Yields and Properties of Acetylhydrazones 122

Table 13 Properties of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines 123

Table 14 ^{13}C Chemical Shifts (ppm) of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines 124

Table 15 The Spectroscopic Data of the Products of Thermolysis of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines 130

Table 16 ^{13}C Chemical Shifts (ppm) of Enol Ethers 88 and 89 131

Page

Table 17 Kinetics of Decomposition of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines at 79°C 134

Tables 18, and 19 Effect of Initial Concentration of $\phi_2\underset{OH}{C}N{=}NCH(CH_3)_2$ on the Yield 156-157

Tables 20-29 Effect of Concentration of Phenol on the Yield 157-162

Table 30 Kinetics of Decomposition of tert-Butylazodiphenylmethyl Acetate at 35°C, in Air 164

LIST OF FIGURES

FIGURE Page

I Plots of % Yield of the Adduct vs. Concentration of Phenol in the Reactions of $\phi_2\underset{\mathrm{OH}}{\mathrm{C}}\mathrm{N{=}N{-}CH(CH_3)_2}$ (0.348 M) with Crotonaldehyde 103

II Plots of % Yield of the Adduct vs. Concentration of Phenol in the Reactions of $\phi_2\underset{\mathrm{OH}}{\mathrm{C}}\mathrm{N{=}N{-}CH(CH_3)_2}$ (0.348 M) with Acrylonitrile 104

III Plots of % Yield of the Adducts vs. Initial Concentration of $\phi_2\underset{\mathrm{OH}}{\mathrm{C}}\mathrm{N{=}N{-}CH(CH_3)_2}$ 105

IV Plots of % Yield of the Adducts vs. [Olefin]/[$\phi_2\underset{\mathrm{OH}}{\mathrm{C}}\mathrm{N{=}N{-}CH(CH_3)_2}$] 106

V The E.S.R. Spectrum of Phenyl-tert-butylnitroxide 113

VI The E.S.R. Spectrum of Di-phenylnitroxide 114

VII The E.S.R. Spectrum of 2-Hydroxyethylphenylnitroxide 115

VIII The E.S.R. Spectrum of Isopropylphenylnitroxide 116

IX The E.S.R. Spectrum of Methylphenylnitroxide 117

X The E.S.R. Spectrum of Allylphenylnitroxide 118

XI The E.S.R. Spectrum of Cyclohexylphenylnitroxide 119

CHAPTER 1

FREE RADICAL CHEMISTRY[1]

1.1 Introduction

In the history of Chemistry, free radicals have been encountered since 1900. We define a free radical here as an atom, molecule or complex which contains one or more unpaired electrons. Although the largest number of radicals are those with an odd electron associated with carbon atoms, halogen atoms and radicals with odd electrons on oxygen, nitrogen, phosphorus, sulphur and silicon play important roles in many reactions. This thesis is concerned only with organic free radicals.

The first authenticated free radical, triphenylmethyl, was discovered by Gomberg in 1900.[2] More and more 'stable' radicals[3] were discovered in the years following Gomberg's initial work.

The role of radicals as transient intermediates in chemical reactions was rapidly recognized as a result of Paneth's[4] discovery of a method of identifying transient radicals. During the 1930's, radical intermediates were proposed for numerous gas-phase reactions by many chemists. Particularly important was the book by Rice and Rice,[5] "The Aliphatic Free Radicals" published in 1935.

Three significant publications appeared in 1937 that might be considered to have launched modern free radical chemistry. A review article by Hey and Waters[6] interpreted a number of reactions as being free radical processes. Kharash[7] proposed the presently accepted free radical chain mechanism for the abnormal addition of hydrogen bromide to alkenes. Flory[8] published a brilliant and prescient paper on the kinetics of vinyl polymerization in terms of a free radical chain reaction.

Since 1937, knowledge of free radical chemistry has increased at a steady accelerating pace both in industrial and academic laboratories.

1.2 Production of Radicals

Three general methods for the production of radicals are mentioned briefly in the following paragraphs.

1.2.1 Thermal Homolysis

At sufficiently high temperatures, all chemical bonds will break to form radicals, but in the temperature range of ordinary solution chemistry, about 15-150°C, the bonds that will do so at reasonable rates are limited to a few types, the most common of which are the peroxy bond and the azo linkage.[9] Substances that produce radicals easily in a thermal process are designated as initiators. Equations [1] to [3] depicted below, illustrate a few typical examples.

[1] $({}^{t}BuO)_2 \rightarrow 2\,{}^{t}BuO\cdot$

[2] $({}^{t}BuOCO_2)_2 \rightarrow 2\,{}^{t}BuO\cdot + 2CO_2$

[3] $(CH_3)_2C(CN)N{=}NC(CN)(CH_3)_2 \rightarrow 2(CH_3)_2\dot{C}CN + N_2$

The ready decomposition of peresters and azo compounds can be attributed to the formation of very stable products (CO_2 and N_2, respectively) which supplies a strong driving force for the dissociation process:

$$R\text{-}N{=}N\text{-}R' \rightarrow R\cdot + R'\cdot + N_2$$

or

$$RCO_2CO_2R' \rightarrow 2CO_2 + R\cdot + R'\cdot$$

It is clear that increasing stability of R· (or R'·), decreases the activation energy for the decomposition. Thus, for the series of azo compounds R-N=N-R a high temperature is required for dissociation when R· are primarily alkyl radicals whereas decomposition becomes much more facile if R· is benzhydryl or triphenylmethyl, which are resonance stabilized. Strongly stabilized radicals so generated may, however, be too unreactive to be of use for initiating radical chains.

Generally there are three modes of decomposition, namely induced decomposition, unimolecular concerted, and unimolecular nonconcerted decompositions. The induced decomposition is a chain reaction arising because the radical products of an initial unimolecular decomposition can attack unreacted initiator molecules to yield new radicals that continue the chain. Numerous examples of the induced decomposition have been reported in the literature; a specific example is given by Benson who studied the decomposition of tert-butyl hydroperoxide.[10] The chain nature of decomposition is amply confirmed by the kinetics,[10] and by the observation that it is accelerated by the addition of an independent source of radicals.[11]

Although azo compounds have been used as a source of free radicals for many years, the induced decomposition of azo compounds to free radicals is rare. Potential mechanisms for induced decomposition of azo compounds include radical substitution at an atom situated α (equation [4]) or β (equation [5]) to azo nitrogen. Azo compounds which are reported to react

$$[4] \qquad R\cdot + X\text{-}N{=}N\text{-}R_1 \rightarrow RX + N_2 + R_1\cdot$$

$$[5] \qquad R\cdot + X\text{-}Y\text{-}Z\text{-}N{=}N\text{-}R_1 \rightarrow RX + YZ + N_2 + R_1\cdot$$

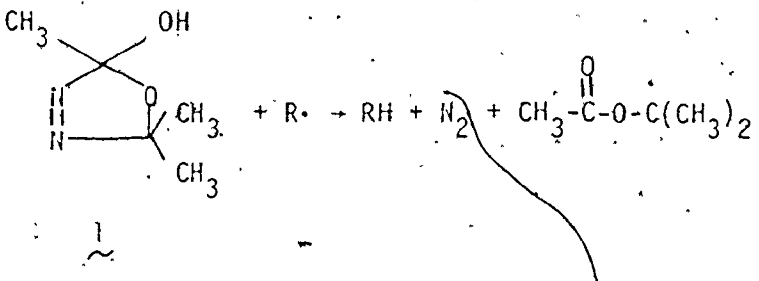
according to equation [4] or [5] are rare. One reason for the rarity may be due to the fact that many azo compounds do not have a reactive site X (equations above), susceptible to radical attack. Several examples of azo compounds which may decompose according to equation [4] have been reported. They are: X = H,[12] X = RCO,[13] X = RSO_2,[14] X = RCO_2,[15] X = ArS,[16] X = CH_3O,[17] and X = Cl.[18] In some of the latter systems, there are other major reactions and radical substitution was not established or suggested as a competitive process.

Few cases of induced decomposition by radical substitution γ to azo nitrogen (equation [5]) have been reported. Benson and his co-workers[19] reported that HCl accelerates the thermal decomposition of azo isobutane and suggested the sequence of reactions in equation [6] below.

$$[6] \quad \begin{array}{l} Me_3C\cdot + HCl \rightarrow Me_3CH + Cl\cdot \\ Cl\cdot + Me_3CN{=}NCMe_3 \rightarrow HCl + \cdot CH_2Me_2CN{=}NCMe_3 \\ \cdot CH_2Me_2CN{=}NCMe_3 \rightarrow CH_2{=}CMe_3 + N_2 + Me_3C\cdot \end{array}$$

Another example is provided by Knittel and Warkentin[20] in this laboratory. They found that 2-hydroxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline 1 decomposes via a concerted, radical-chain mechanism (equation [7]). The concerted induced decomposition of 1 by attack at hydroxyl hydrogen is confirmed by spin trapping with nitrosobenzene, reactions with olefins, inhibition of decomposition by triphenylstannane, and initiation of decomposition by 'stable' free radicals.

[7]



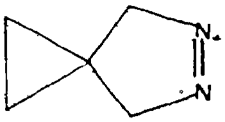
1

For the latter two modes of decomposition (concerted or stepwise cleavage), we use the decomposition of azo compounds as an illustration. In a concerted reaction (equation [8]), two C-N bonds would break simultaneously, whereas a stepwise process would produce first one R· radical and later the second (equation [9]).

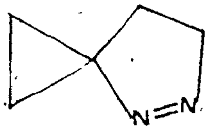
[8] $R{-}N{=}N{-}R_1 \rightarrow R\cdot + N_2 + R_1\cdot$

[9] $R{-}N{=}N{-}R_1 \rightarrow R\cdot + \cdot N{=}N{-}R_1 \rightarrow N_2 + R_1\cdot$

The mechanism of the decomposition of azo compounds has been investigated for many years by several workers. Earlier kinetic studies of azo thermal decomposition[21] led to the conclusion that the rate-determining step involves simultaneous rupture of both C-N bonds. The decomposition of symmetric 3,5-diaryl-1-pyrazolines having para-chloro, para-methoxy and para-hydrogen substituents was investigated by Overberger,[22] and he postulated a concerted, homolytic decomposition to a biradical-intermediate mechanism. McGreer[23] has studied the thermal decomposition of 1-pyrazolines that have electronegative substituents at position three, and he suggested that only one bond breaks in the initial transition state to give a zwitterion. Seltzer[24] found by studying secondary deuterium isotope effects that in unsymmetric azo compounds, one bond rupture occurs. Pryor and Smith[25] have found independent evidence favouring the single bond cleavage mechanism for unsymmetric azo compounds. Neuman[26] found by measuring the activation volumes that azo compounds undergo either concerted or stepwise homolytic decomposition. Crawford[27] has proposed that not only unsymmetric but also some symmetric azo compounds decompose in the gas phase by the one bond scission pathway. Kopecky[28] suggested that the thermolysis of cis- and trans-3,6-diphenyl-3,4,5,6-tetrahydropyridazine is by simultaneous cleavage of both C-N bonds. More recently, Bergman[29] found that the symmetrical cyclic azo compound 2 decomposes by simultaneous rupture of both C-N bond, while the unsymmetrical one 3 decomposes by sequential C-N cleavage.



2



3

As reviewed above, the mechanism of decomposition of cyclic azo compounds appears to be very difficult to generalize and seems to be strongly altered with changes in structures such as the size and nature of the ring involved. The thermolysis of a specific class of five-membered azo compound, oxadiazolines, will be discussed in Chapter 4.

Decomposition of azo compounds is potentially complicated by the existence of cis and trans isomers. The trans form is the more stable; cis isomers can be prepared by low temperature photolysis, but they decompose fairly rapidly at room temperature to yield partly trans isomer and partly radical products.[30] The cis isomers have been implicated as intermediates in photochemical decompositions starting from trans,[30] but it is not clear whether they are also involved in thermal decomposition.

Besides peroxides and azo compounds, organometallic compounds of such metals as mercury and lead undergo thermolysis and are also used as radical sources. However, they are highly toxic which then limits their use both in industries and in laboratories.

1.2.2 Irradiation

Radicals can be photo-generated. Most bonds encountered in organic compounds have energies of the order of 50-90 Kcal·mole^{-1}. Light energy of this magnitude is used to effect bond scission. Provided the substance can absorb the radiation, visible or ultraviolet radiation is of sufficient energy to cause rupture of most types of bonds. Even when this proviso is not met, the energy transfer can be promoted by a 'photosensitizer'. Photosensitization is the process by which the energy absorbed by one molecule is transferred to another by collision and leads to reaction of the latter. Benzophenone, for instance, is a very good triplet photosensitizer in photochemistry. Examples of photolyses which generate radicals are given in equations [10] to [12].

[10] $ROOR \rightarrow 2RO\cdot$

[11] $RN{=}NR \rightarrow 2R\cdot + N_2$

[12] $ROCl \rightarrow RO\cdot + Cl\cdot$

Two advantages of photogeneration of radicals should be mentioned: (a) the reaction may be carried out at any convenient temperature, and (b) specific bond scissions can be done by radiation of a particular energy to the molecule under study. However, the disadvantage of possible light-sensitivity of the reaction products must be noted.

1.2.3 Redox Reactions

An important and extremely versatile means of producing free radicals (chiefly in aqueous systems) and inducing radical chain processes is the use of partially or wholly inorganic oxidation-reduction systems.[1f] An earlier and good example is the reaction of hydrogen peroxide with Fe(II) ion (Fenton reaction,[31,32] equation [13]).

$$[13] \quad H_2O_2 + Fe(II) \rightarrow Fe(III) + OH^- + \cdot OH$$

Electrochemically, the Kolbe reaction involving the oxidation of carboxylates is undoubtedly the best-known and most extensively studied example of anodic oxidation[33] (equation [14]).

$$[14] \quad RCO_2^- \xrightarrow{-e} RCO_2\cdot \rightarrow R\cdot + CO_2$$

$$R\cdot + R\cdot \rightarrow R\text{-}R$$

1.3 Detection of Free Radicals by the Spin-Trap Technique

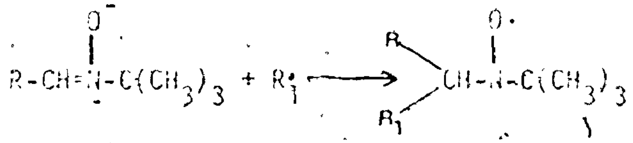
Reactive free radicals play a role in many reactions, and electron spin resonance spectroscopy is by far the most useful method of radical detection. Detailed analysis of an e.s.r. spectrum frequently makes it possible to deduce not only the gross chemical structure of the radical but also its conformation. Spin densities at various positions in delocalized radicals may also be obtained. The sensitivity of the method allows radical concentrations of 10^{-8} M to be observed.

For a detailed treatment of the theory and practice of e.s.r., reference should be made to a specialized text by Carrington.[34] This section only outlines a physical method of detecting radicals, with e.s.r. techniques, by so-called spin trapping. Other physical methods of detection such as magnetic susceptibility, CIDNP, mass spectrometry, etc. are not included here, but references should be made to any standard texts.[1]

Transient free radicals may be detected and identified directly by e.s.r. only if the radicals are produced in relatively high concentrations in the e.s.r. cavity by intense in situ irradiation[35,36] or by rapid-mixing flow systems.[37] Sometimes e.s.r. equipment has been substantially modified to increase sensitivity and resolution. Several groups of workers[38-43] more or less simultaneously have solved this problem by carrying out the particular reaction in the presence of a suitable diamagnetic compound, called a spin trap by Janzen, which can trap a transient radical giving rise to a stable radical. The e.s.r. spectrum of the latter may be obtained without recourse to special techniques.

Suitable spin traps include nitrones 4 and nitroso compounds 5, both of which on reaction with radicals give rise to nitroxides 6 and 7 (equations [15] and [16]). For different aspects of the chemistry of nitroxides, the reader is referred to several good texts[44-46] and reviews.[47-50] The most commonly used nitrones are phenyl tert-butyl nitrone 4a and the unsubstituted t-butyl nitrone 4b. The nitroso compounds used as spin traps are nitroso-tert-butane 5a, 2-methyl-2-nitroso-3-butanone 5b and nitrosobenzene 5c.

[15]



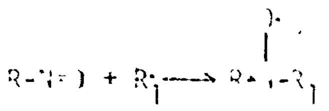
$$R\text{-}CH{=}\overset{O^-}{\underset{+}{N}}\text{-}C(CH_3)_3 + R_1^{\bullet} \longrightarrow \underset{R_1}{\overset{R}{>}}CH\text{-}\overset{O\cdot}{N}\text{-}C(CH_3)_3$$

4 6

a:R = C_6H_6

b:R = H

DTIC COPY

[15] 

$$R\text{-}N{=}O + R_1\cdot \longrightarrow R\text{-}\overset{O\cdot}{\overset{|}{N}}\text{-}R_1$$

5 7

a:R $(CH_3)_3C$

b:R $CH_3COC(CH_3)_2$

c:R C_6H_5

analysis of the e.s.r. spectra of the resultant stable nitroxide radicals can give information about the nature of the transient radical. The spectra of nitroxides are characterized by a 1:1:1 triplet due to splitting by ${}^{14}N$, the value of the splitting constant (a_N) depending on the nature of the groups attached to nitrogen. This triplet is further split as a result of coupling with magnetic nuclei on the α- and β-carbon atoms. In many cases, the nitroxide derivative is already known and only comparison is required, but in others identification depends on more general experience. The a_N is now known[39] to be 10-15 gauss for trapped alkyl radicals, nearly 30 gauss for alkoxy radicals and only 6-8 gauss for acyl radicals. In the case of nitrones, $a_{\beta\text{-}H}$ can also be used. It is usually 2-3 gauss, but now the hydrogen atoms are fairly remote from the radical centre, making it more difficult to identify the radical if its splittings are not already known. Therefore, the suspected nitroxide is made by an independent route for direct spectral comparison.

The ideal trap is one in which the hyperfine splitting of the derived nitroxide radical is due entirely to magnetic nuclei in the transient radical. For this reason, 2-methyl-2-nitrosopropane has been used extensively by Perkins.[49] However, it suffers a disadvantage of being photochemically and thermally unstable. As pointed out by Janzen,[43] there are both advantages and disadvantages inherent in the use of either nitrones or nitroso compounds as traps; the technique of spin-trapping has to be used with caution.

Various alternative spin traps have recently been found in the literature, among them nitrobenzene,[51] N-nitroso compounds,[52] hindered phenols,[53] 1-nitrosoadamantane,[54] benzonitrile-N-oxide[55] and anion$[CH_2NO_2]^-$.[56]

Recently, several reviews have been published[57-59] to discuss the use of nitroxide radicals as spin labels to probe the structure and function of biological macromolecules.

Before concluding this section, one further point to be made is that the detection of a particular radical does not necessarily mean that it is involved in the major reaction pathway in the system under study. Thus, even though N-bromosuccinimide has been shown to give succinimidyl radicals, it is almost certain that these are not involved to a major extent in the allylic bromination of alkenes.[49]

1.4 Classification of Radical Reactions

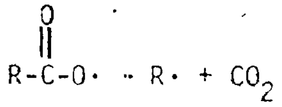
Radical reactions can be classified into different types, and these are summarized in the following paragraphs.

1.4.1 Unimolecular Reactions

1.4.1.a Radical Fragmentations

Radical fragmentations, sometimes referred to as β elimination, occur both in solution and in the gas phase, particularly at low pressure. They may be looked upon as the reverse of radical additions. Typical examples are given below [equations [17] and [18]).

[17] $(CH_3)_3\dot{C}O \to CH_3\cdot + (CH_3)_2C{=}O$

[18] 

$\mathrm{R{-}\overset{\overset{O}{\|}}{C}{-}O\cdot \to R\cdot + CO_2}$

These processes are usually endothermic and are favoured by an increase in temperature. The major driving force is derived from the resulting increase in entropy since the formation of two species from one brings about an additional translational degree of freedom. Fragmentation of a cyclic radical results also in an entropy increase, in this case due to enhancement in rotational degrees of freedom.

Radical ions also undergo fragmentation (equation [19]).

[19] $PhCH_3^{\cdot+} \to PhCH_2\cdot + H^+$

1.4.1.b. Radical Rearrangements

The subject of radical rearrangements has been reviewed in several texts and many review articles, despite the scarcity of this reaction compared to carbonium ion rearrangements. Most importantly, the classic reviews of Walling[60] and Freidlina,[61] and recently by Wilt[62] should be consulted. Of these the 1,2-halogen shift and the 1,2-phenyl shift are common. Examples are given in equations [20] to [22].

[20] $PhCMe_2\dot{C}H_2 \to Me_2\dot{C}CH_2Ph$

[21] $Me_2CBr\dot{C}H_2 \to Me_2\dot{C}CH_2Br$

[22] $Cl_3C\dot{C}HCH_2Br \to \dot{C}Cl_2CHClCH_2Br$

Some years ago, two groups of workers[63] gave a theoretical rationale (based on LCAO molecular orbital calculations) for the more difficult nature of radical rearrangements compared to their cationic analogs. Cationic rearrangements fill the bonding molecular orbital only and the transition state is totally bonding. On the contrary, radical (and anionic) rearrangements must have some antibonding character in the transition state because the orbital at the reactive centre is not empty.

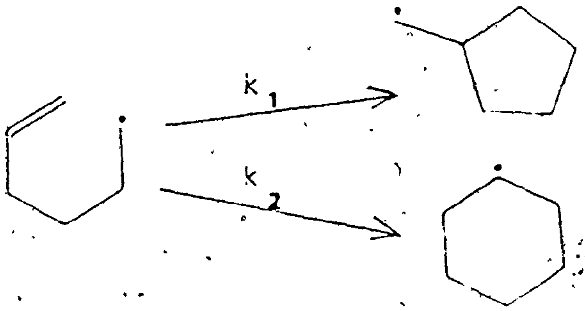
Carbonium ion rearrangements are widespread, and radical rearrangements would be expected to be limited in number. Moreover, truly 1,2-carbanion rearrangements have not been and perhaps never will be observed.

No radical rearrangements involving 1,2-alkyl or hydrogen migration have been known to occur, although the latter has been proposed from time to time.[62]

1.4.1.c Radical Cyclizations

Radical cyclizations may be regarded as intramolecular additions to double bonds. Such reactions are very sensitive to the stereoelectronic requirement of the transition state.[64] A large number of examples are known in cyclization of hex-5-en-1-yl radicals;[65] they can either cyclize to cyclopentylmethyl or cyclohexyl radicals (equation [23]).

[23]



The hex-5-en-1-yl radical cyclizes almost exclusively to give the less stable of the two possible radicals, namely the cyclopentylmethyl radical rather than the cyclohexyl radical, i.e., the reaction gives the thermodynamically less stable radical. This cyclization is subject to kinetic control, as both the cyclopentylmethyl and cyclohexyl radicals show no tendency to fragment,[66] and hence one can say k_1 k_2.

1.4.2 Bimolecular Reactions between Two Radicals

1.4.2.a Combinations

Combination of two radicals leads to bond formation and is therefore energetically favourable. The process is known to be extremely fast requiring little or no activation energy, but since in solution the concentrations of radicals are extremely low and reactions between them depend on the square of their concentrations such a process is in general not as important as transfer reactions with the solvent. However, combination reactions are radical destroying processes and constitute one of the termination pathways in chain reactions. Also, they may predominate in the case of a relatively stable radical, such as free benzyl, which is not reactive enough to attack other molecules present in the system, and persists in solution until it collides with a like radical and couples with it to yield the 'dimer'. Examples are given in equations [24] to [26].

[24] $PhCH_2\cdot + PhCH_2\cdot \rightarrow PhCH_2CH_2Ph$

[25] $PhCH_2\cdot + Me_3C\cdot \rightarrow PhCH_2CMe_3$

[26] $PhS\cdot + PhS\cdot \rightarrow PhSSPh$

Combination may take place readily in a solvent 'cage'. When generated in solution from a radical initiator by bond cleavage, radicals are always formed in pairs in close proximity to each other, within a solvent cage, and do not immediately separate. Before diffusing out of the cage, they may undergo collision with each other and combine to regenerate the initiator or give other products. This type of reaction has been called a 'cage reaction'. A detailed treatment of the cage effect is given in a recent article by Koenig.[67] The ratio of radical pairs reacting in the ~~solvent~~ cage, by combination or disproportionation, to the total number of pairs formed is called the cage effect. The caged radical-pair phenomenon nowadays is the accepted theory of chemically induced dynamic nuclear polarization (CIDNP). The theory and application of CIDNP are not discussed here; readers are referred to several good articles.[68-72]

1.4.2.b Disproportionations

These reactions involve the transfer of a hydrogen atom from one radical to another. For example, two tert-butyl radicals can disproportionate to yield isobutane and isobutene (equation [27]).

[27] $(CH_3)_3C\cdot + (CH_3)_3C\cdot \rightarrow (CH_3)_3CH + CH_2{=}C(CH_3)_2$

The disproportionation process, like combination, is a very exothermic reaction since two bonds are formed and only one is broken. In a termination process, disproportionation always competes with combination reactions.

1.4.3 Bimolecular Reactions between Radicals and Molecules

1.4.3.a Substitutions

Free-radical substitution reactions are defined operationally as homolytic processes in which one atom or group of atoms in a molecule is replaced with another (equation [28]) without regard to details of mechanism.

[28] $R\cdot + AB \rightarrow RA + B\cdot$

Substitution reactions are usually chain reactions consisting of successive repetitions of individual transfer steps. There are two types. In the S_H1 reaction (unimolecular homolytic substitution), homolysis of AB is rate-determining and is followed by radical coupling (equation [29]). An example[73] would be the formation of coupled products

[29] $$Ab \xrightarrow{\text{slow}} A\cdot + B\cdot$$

$$R\cdot + A\cdot \xrightarrow{\text{fast}} RA$$

from decomposition of a perester in the presence of a stable radical such as galvinoxyl. However, S_H1 reactions are comparatively rarer than S_H2 (bimolecular homolytic substitution) reactions in which there is direct bimolecular interaction between the radical and the transfer agent.

S_H2 reactions can be subdivided into two types, synchronous (equation [30]) and stepwise (equation [31]). The distinction between

[30] $$R\cdot + AB \rightarrow \underset{\text{Transition State}}{[R{-}{-}{-}A{-}{-}{-}B]^{\ddagger}} \rightarrow RA + B\cdot$$

[31] $R\cdot + AB \rightarrow (RAB)^{\cdot} \rightarrow RA + B\cdot$

Intermediate

these two types would depend on the behaviour of the adduct radical $(RAB)^{\cdot}$. If the adduct radical has a finite lifetime, the substitution is stepwise; otherwise, the reaction is synchronous. Numerous examples of S_H2 reactions of organic, organometallic and inorganic compounds can be found in a specialized book by Ingold.[74]

Radical attack is most common at monovalent halogen[75] and hydrogen[76] (see later) atoms. Attack at polyvalent atoms is less prevalent but has been clearly demonstrated for oxygen, sulfur, phosphorous, and several of the metals.[74] Attack at saturated carbon is very rare,[74] but addition-elimination sequences at unsaturated carbon are well known.

1.1.3.b Abstractions

Abstraction reactions are specific types of substitution reactions (above). Two most common abstraction reactions of radicals are halogen[75] and hydrogen[76] abstractions. The former abstraction will not be discussed here, but readers are referred to the article cited. Also, it is not intended to draw together information on the abstraction of hydrogen from a variety of environments.[76-78] Discussion will be mainly based on the hydrogen transfer from alcohols.

A wide variety of radicals, e.g., alkyl,[79] alkoxy,[80-82] hydroxyl,[83] nitrogen,[84,85] and sulphur[86] radicals, abstract hydrogen from alcohols. In solution, the majority of alcohols are preferentially attacked by free radicals at the α-CH bond (D, 93 Kcal mole^{-1}) and not the O-H bond (D, 103 Kcal mole^{-1}), with the exception of tertiary alcohols.[81,82]

The resulting α-hydroxyalkyl radicals have been trapped by olefins and their e.s.r. spectra examined.[82,87-91]

Abstraction of the hydroxylic proton has been less commonly observed.[92] A few cases have been reported of hydrogen abstraction from the hydroxyl group. The $Me_2C{=}\dot{C}H$ radical abstracts[93] deuterium from deuterioethanol (EtOD). Some cyclopropanols[94] on oxidation or other reaction give products consistent with the formation of alkoxyl radicals. Diphenylphosphino-radicals have been found[95] to abstract the hydroxylic proton by way of an initial attack upon the oxygen atom. It has been demonstrated by Ingold,[91] and independently by Kochi,[82] that a hydrogen atom can be transferred from the hydroxylic group of an alcohol to an alkoxy radical. Warkentin[20] recently found that a variety of radicals can abstract hydroxyl hydrogen efficiently from a special type of α-azocarbinol **1**. Gray and Herod[96] found the α-C-H position of ethanol at 150 C to be twice as reactive at the O-H site toward methyl radicals.

1.4.3.c Additions

Among radical reactions, the addition reactions are the most intensively studied and best understood. Besides being of great theoretical interest,[97-99] they have assumed great practical importance because of their versatile applications in organic synthesis.[100-106] Here, we only discuss the addition reactions with unsaturated compounds yielding small molecules. For detailed treatment of addition reactions generating giant molecules, the reader is referred to the standard texts by Walling[1a] and by Vollmert.[107]

Stoichiometrically simple additions to unsaturated compounds can be represented as in equation [32], in which the reagent added is symbolized X-Y.

[32] $X\text{-}Y + AB \rightarrow AXBY$

Various radicals will undergo addition reactions with many unsaturated compounds (AB above) such as olefins, acetylenes, aromatic compounds, azo compounds, and carbonyl compounds. The addition reaction with olefins is by far the most extensively investigated. Reagents[1a,1b,3-13b] which undergo radical additions to suitable unsaturated linkages include halogens, HBr, hydrocarbons, polyhaloalkanes, alcohols, ethers, amines, aldehydes, ketones, esters, aliphatic acids, and compounds of sulphur, phosphorous, silicon, tin, germanium, and other elements.

The radical addition mechanism is a complex sequence of steps, as shown in Scheme I. Addition to olefins is taken as an example.

Scheme I

Initiation:

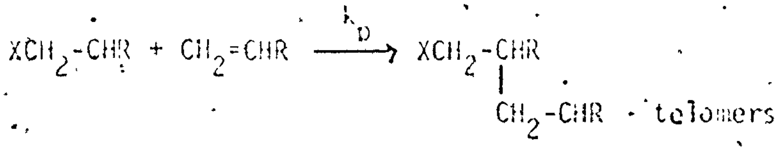
[33] $XY \rightarrow X\cdot + Y\cdot$

Propagation:

[34] $X\cdot + CH_2\text{=}CHR \rightarrow XCH_2\text{-}\dot{C}HR$

[35] $XCH_2\text{-}\dot{C}HR + XY \xrightarrow{k_{tr}} XCH_2CYHR + X\cdot$

[36]



$$XCH_2\text{-}\dot{C}HR + CH_2\text{=}CHR \xrightarrow{k_p} \begin{array}{l} XCH_2\text{-}CHR \\ \quad\;\; | \\ \quad\;\; CH_2\text{-}\dot{C}HR \rightarrow \text{telomers} \end{array}$$

Termination:

[37] $2X\cdot \rightarrow X-X$

[38] $X\cdot + XCH_2\dot{C}HR \rightarrow XCH_2CHXR$

[39] $2XCH_2\dot{C}HR \rightarrow$ dimer or disproportionation

The kinetic aspects of the above sequence are discussed in section 2.7.

The chain sequence can be started both by radical initiation and photoinitiation. Data about the initiation step are sparse. This is because in most radical chain reactions the average kinetic chain lengths are very long and consequently the initial source of radicals has little influence on the nature of the addition products.

In most radical addition reactions, the 1:1 adduct is formed in the propagation steps of the chain sequence. A significant complication could arise in additions from the circumstance that the intermediate radical $XCH_2-\dot{C}HR$, instead of undergoing transfer to carry on the chain, could add to another olefin molecule (equation [36]) to give a new radical $XCH_2CHRCH_2\dot{C}HR$, which, by a repetition of this process, leads to a chain polymer or "telomer". This side reaction, telomerization, should not be serious if both of the propagation steps (equations [34] and [35]) are exothermic and rapid compared with all chain termination steps. The reactivity ratio, k_{tr}/k_p, referred to as the chain-transfer constant, is a measure of the reactivity of the adding reagent with respect to that of the unsaturated compound toward reaction with the adduct radical. A system with a high chain-transfer constant (k_{tr}/k_p > 10) results in high yields of the simple 1:1 addition product, whereas a system with a low chain-transfer constant (k_{tr}/k_p < 1) will give mainly telomeric products under the same conditions.[16] Walling[11] has derived approximate energies of the propagation steps in a number of radical addition reactions and, from these values, it can be predicted whether or not radical chain processes involving addition reactions are efficient.

It has been found by Minisci[104] that many telomerization problems can be overcome if a redox system is present in the addition reaction mixture. This is usually supplied by having present a metal cation such as Fe^{3+} or Cu^{2+}. Such salts can greatly affect the course of radical additions to olefins and the nature of the products obtained. A redox system generally does not affect k_p, but it can promote k_{tr} very considerably and thus the chain-transfer constant will be increased.

The chain sequence can be terminated in various ways depending on the system involved. In general, chain termination occurs by radical destroying processes such as dimerization or disproportionation. These two reactions we have discussed previously (section 1.3.[illegible]).

As to whether the addition step (equation [34]) is reversible or otherwise may be inferred from cis-trans isomerization which the olefins may undergo during the reaction. Isomerization in all likelihood arises from free rotation within the intermediate radical XCH_2-ĊHR, provided that this occurs faster than its reaction with the addendum XY. Reversible reactions have been demonstrated in a number of cases such as addition reactions with halogen atoms,[108,109] thiyl radicals[110-112] and organometallic radicals.[113,114]

Another complication in radical addition processes may arise from the possibility of competition between the desired addition (equation [31]) and displacement reaction between the radical X· and the olefin, depicted below (equation [40]). Here, attack upon allylic hydrogen atoms is

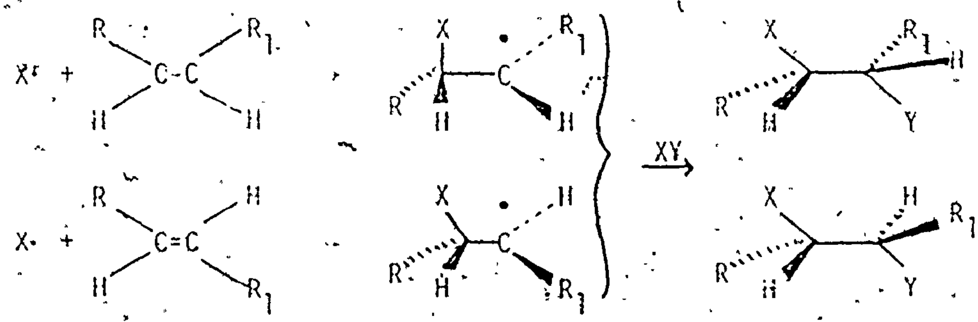
[40] $X\cdot + CH_2{=}CHCH_2R \rightarrow XH + CH_2{=}CH\dot{C}HR$

particularly likely because the resulting allylic radical is a highly resonance stabilized species. That stabilization means that allylic radicals are unreactive toward the addend XY, and instead accumulate in the system until they are destroyed by radical coupling or disproportionation reactions.

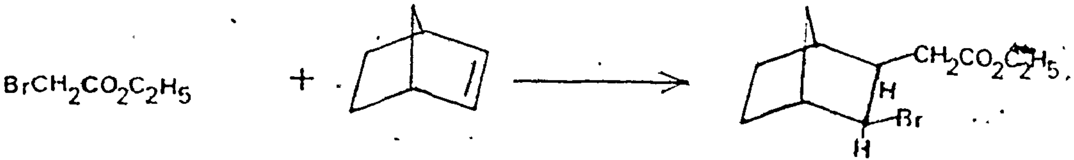
Stereochemically, different possible stereoisomers can be obtained from radical additions to suitably substituted olefins. From open-chain olefins, in general, both erythro and threo pairs are obtained starting either from the cis- or trans-olefins. The presumed explanation is that the intermediate radical undergoes free rotation about the former double bond at a rate which is rapid compared with reaction with the addend XY (equations [41] and [42]).

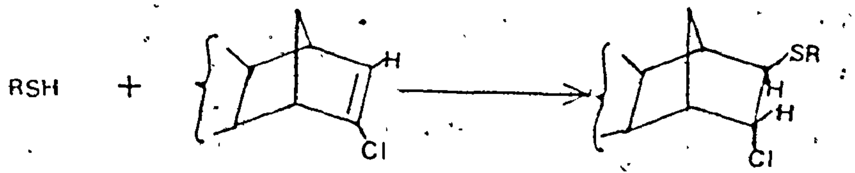
[41]

[42]



The stereochemistry of carbon radical additions to cyclic olefins has not been studied. However, the addition of hydrogen bromide and of mercaptans is preferably trans,[115-117] and a similar result might be expected with carbon radicals. Additions to the bridged norbornene system in contrast appear to give solely the cis-exo product, presumably for steric reasons (see later), e.g., with ethyl bromoacetate[118] (equation [43]) and thiols[119] (equation [44]). Conjugated dienes generally

[43]


[44]


add free-radical reagents in a 1,4 manner, but the relative amounts of cis and trans products have not been investigated in detail.[103]

Brief mention of the orientation of radical addition is appropriate. Free-radical addition is seldom completely specific to one carbon atom of the double bond, but the predominant direction of attack can nearly always be predicted by the simple empirical rule that the first-added species will attack at the 'least substituted' carbon atom. For all radicals so far studied, this rule appears to hold with few exceptions, irrespective of the nature of substituents on the olefin. The exception,[120,121] for example, is 1,1-difluorochloroethylene where both $CF_3\cdot$ and $CCl_3\cdot$ radicals react faster at the $=CF_2$ end.

The orientation of radical addition has been interpreted in terms of four main factors: (i) the strength of the bond being formed, (ii) steric hindrance, (iii) polar effects, and (iv) stability of the addend radicals. These factors will be discussed in section 2.6.

For more details of orientation of radical addition reactions, the reader is referred to several articles by Haszeldine,[120] Cadogan,[122] Walling,[101] Husang,[123] Tedder,[121,124] and Kerr.[125]

In the following paragraphs, the addition of hydrocarbons and alcohols across double bonds, and the radical additions to the azo N=N linkage are discussed briefly.

Very few hydrocarbons are known to add to olefins effectively. One reason for the ineffective addition of hydrocarbons, e.g., alkane, to olefins may be the unfavourable thermochemistry of chain transfer steps. It is illustrated in terms of radical chain addition of isobutane to acrylonitrile (equations [45] and [46]). The addition is impractical

[45] $Me_3C\cdot + CH_2{=}CHCN \rightarrow Me_3CCH_2\dot{C}HCN$

[46] $Me_3CCH_2\dot{C}HCN + Me_3CH \rightarrow Me_3CCH_2CH_2CN + Me_3C\cdot$

because the second chain carrying step is too endothermic (equation [46]).

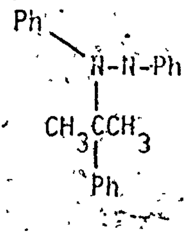
To our knowledge, only two examples of addition of hydrocarbons to olefins are known. The first example was given by Hey[126] who reported that cyclohexane, under modified conditions, gives with 1-octene a 40% yield of 1-cyclohexyloctane. The other example was provided by Huang,[127] who obtained the 1:1 adduct, no less than 59%, from the addition of toluene to methyl crotonate.

Primary and secondary alcohols add to olefins to form secondary and tertiary alcohols, respectively. The α-hydrogen of alcohols is susceptible to abstraction (equation [47]), and the resulting radical is capable of reaction with olefins in a chain process as in Scheme I (page 19).

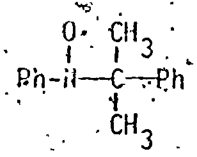
[47] $R_2CH\text{-}OH + R_1\cdot \rightarrow R_2C\text{-}OH + R_1H$

Tertiary alcohols, having no α-hydrogen atoms, do not add to olefins in a free-radical chain reaction. Chain-transfer constants with simple olefins average near 10^{-2},[128] which means that, except in the presence of substantial excess of the alcohol, telomer formation is the predominant reaction. The tendency toward telomer formation with a given olefin is CH_3OH > primary alcohol > secondary alcohol. With readily polymerized olefins, such as styrene, telomer formation is the nearly exclusive result.

Very few examples are known in the literature of additions across the azo N=N linkage to form substituted hydrazines, via a free-radical chain process. The first example is provided by the addition of benzaldehyde to azobenzene forming 1-benzoyl-1,2-diphenylhydrazine in 80% yield.[129] Wan *et al.*,[130] in 1964, successfully demonstrated the addition of cumene to azobenzene by irradiation; the corresponding substituted hydrazine was isolated. They identified, by e.s.r., the intermediate hydrazyl radical 8 in irradiated solution of azobenzene in cumene. However, Ingold[131] proved that their e.s.r. spectrum was not that of 8, and, in fact, is phenyl cumyl nitroxide 9.

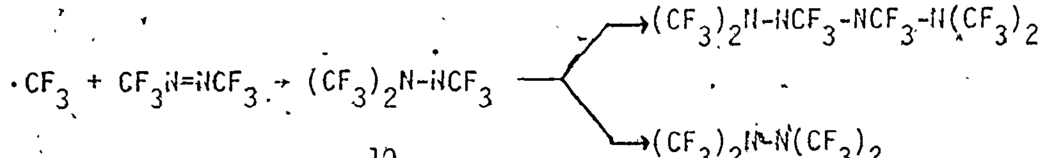


8



9

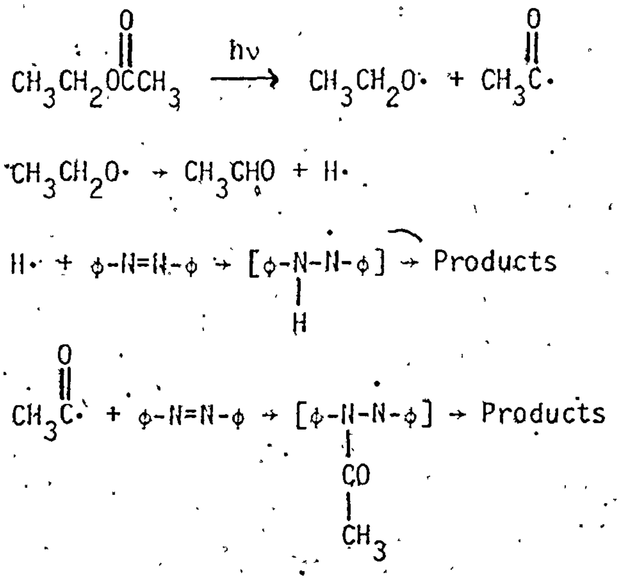
Radical additions to the azo bridge, to form hydrazyl radicals, have been demonstrated in a few instances. Trifluoromethyl radicals are reported to add readily to azotrifluoromethane, forming 1,1,2-trifluoromethylhydrazyl radical 10,[132,133] which then undergoes radical coupling reactions to yield the products (equation [48]).

[48]


$$\cdot CF_3 + CF_3N{=}NCF_3 \rightarrow (CF_3)_2N\text{-}\dot{N}CF_3 \rightarrow \begin{cases} (CF_3)_2N\text{-}NCF_3\text{-}NCF_3\text{-}N(CF_3)_2 \\ (CF_3)_2N\text{-}N(CF_3)_2 \end{cases}$$

10

Cepeiansky[134] has investigated the photolysis of aromatic azocompounds in ethyl acetate solution, and he suggested that the photolysis of azocompounds is caused by attack of radicals, generated during photolysis of ethyl acetate, on the molecules of the azocompound (equation [49]).

[49]


$$CH_3CH_2OC(=O)CH_3 \xrightarrow{h\nu} CH_3CH_2O\cdot + CH_3\overset{O}{\overset{\|}{C}}\cdot$$

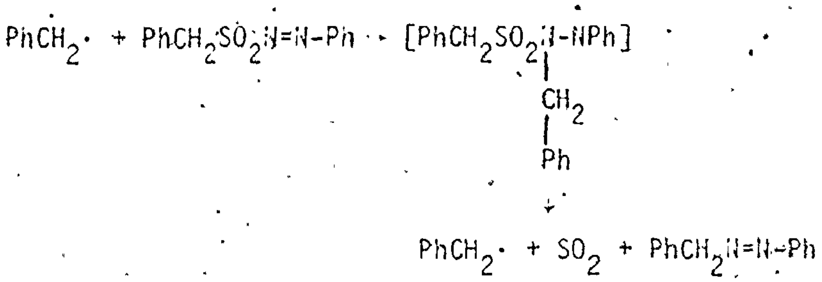
$$CH_3CH_2O\cdot \rightarrow CH_3CHO + H\cdot$$

$$H\cdot + \phi\text{-}N{=}N\text{-}\phi \rightarrow [\phi\text{-}\dot{N}\text{-}N(H)\text{-}\phi] \rightarrow \text{Products}$$

$$CH_3\overset{O}{\overset{\|}{C}}\cdot + \phi\text{-}N{=}N\text{-}\phi \rightarrow [\phi\text{-}N(COCH_3)\text{-}\dot{N}\text{-}\phi] \rightarrow \text{Products}$$

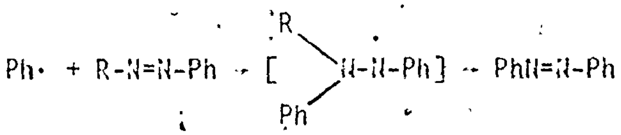
Other examples are given by Kice[135] (equation [50]) and Warkentin[136] (equation [51]). These are, in fact, radical substitution reactions at azo nitrogen.

[50]



$$PhCH_2\cdot + PhCH_2SO_2N{=}N\text{-}Ph \rightarrow [PhCH_2SO_2N(CH_2Ph)\text{-}NPh] \rightarrow PhCH_2\cdot + SO_2 + PhCH_2N{=}N\text{-}Ph$$

[51]



$$Ph\cdot + R\text{-}N{=}N\text{-}Ph \rightarrow [R(Ph)N\text{-}N\text{-}Ph] \rightarrow PhN{=}N\text{-}Ph$$

For details of the chemistry of hydrazyls, reference should be made to two specialized texts.[45,46]

1.4.4 Electron-Transfer Reactions of Radicals

Many radicals undergo oxidation or, less commonly, reduction by the transfer of an electron. This is usually transferred to or from a transition metal. There are two routes available for oxidation of radicals. Kochi[137] has designated these as electron-transfer oxidation (equation [52]) and ligand-transfer oxidation (equation [53]).

[52] $R\cdot + Cu^{2+} \rightarrow R^{+} + Cu^{+}$

[53] $R\cdot + CuCl_2 \rightarrow RCl + CuCl$

The first of these corresponds to an outer-sphere mechanism and the latter to an inner-sphere mechanism in an inorganic system.[138]

It is not intended to discuss this subject in any detail. For more information, the reader is referred to several good review articles.[139-141]

1.5 Some General Characteristics of Radical Chain Reactions

Free radicals, being uncharged entities, are relatively insensitive to polarity of solvents, and, in fact, they behave very similarly in the liquid and gas phases. For example, the decomposition of di-tert-butyl peroxide proceeds at the same rate in the gas phase as in solutions of benzene, cumene, and most other solvents.[142,143]

In contrast to many polar reactions, radical processes (except certain oxidation-reduction systems) rarely show catalysis by acids or bases. On the other hand, the radical reactions are started by some initiating radicals introduced into the system. Compounds which can form free radicals readily, such as hydroperoxides, peroxides, and many azo compounds, promote radical reactions and are known as initiators. In the absence of initiators, the initiation process may come from heat, light, or ionizing radiation.

Radical reactions can be initiated by initiators; conversely, they can also be retarded or inhibited by so-called inhibitors. Inhibitors, in general, are either stable free radicals, e.g., oxygen, nitric oxide or diphenylpicrylhydrazyl (DPPH) or non-radical substrates which react readily with radicals to produce another radical either too stable to enter into the kinetic chain or reactive in some new pathway. Typical inhibitors are phenols, thiols, aromatic amines, quinones and aromatic polynitro compounds, although the effectiveness of an inhibitor varies markedly with the system in which it is employed. Oxygen is well known for its unpredictable effect on radical reactions: small quantities of oxygen may initiate a reaction whereas a large quantity may completely inhibit it. For more information of stable free radicals, reference should be made to a specialized text.[45]

The mechanisms of inhibitor action are complex and not entirely understood.[1d] In general, three mechanisms for inhibition can be visualized:

(i) Inhibition by radicals. An added free radical species will inhibit the processes (equation [54]), if it scavenges X· but does not react with X to convert it to X·.

$$[54] \qquad R\cdot + X\cdot \rightarrow RX$$

$$R\cdot + X \not\rightarrow X\cdot$$

(ii) Atom transfer. Atom transfer is accompanied by inhibition if the transfer agent forms a stable radical that does not reinitiate. An example is transfer by DPPH or phenols, which produces the very stable DPPH or phenoxy radical in the transfer step (equations [55] and [56]).

$$[55] \qquad R_n\cdot + DPPH\text{-}H \rightarrow R_n\text{-}H + DPPH\cdot$$

$$[56] \qquad R\cdot + PhO\text{-}H \rightarrow RH + PhO\cdot$$

(iii) Addition. Some substances add radicals to form stabilized species that do not propagate the kinetic chain. An example is the inhibition of radical polymerization by oxygen (equation [57]).

$$[57] \qquad R_n\cdot + O_2 \rightarrow R_nOO\cdot$$

The chemistry of inhibitors is important both in the study of radical chains and in suppressing unwanted radical reactions.

1.6 Factors Governing Radical Reactions

In general, there are four factors governing the course of radical reactions. Each factor is discussed briefly in the following paragraphs.

1.6.1 Stabilization

A radical can acquire stability in several ways, but largely through normal resonance and σ,π-hyperconjugation. If the system allows sufficient delocalization of the free electron, the radical may become so stable that it refuses to react at all; aryloxy and diphenylpicrylhydrazyl (DPPH·) radicals, are examples. The ability of the radical centre to attain a planar conformation is important with carbon radicals. Deviations from planarity usually decrease the stability of a radical.

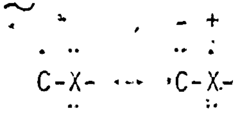
The hyperconjugation effect is well exemplified in the increasing stability from methyl to tert-butyl radicals. The order of increasing radical stability is methyl $<$ primary $<$ secondary $<$ tertiary.

The contribution from the steric factor to stability is well-demonstrated in the triphenylmethyl radical. The stability of this radical is due largely to steric interaction in the dimerization reaction.

1.6.2 Polar Effects

Polar effects in free radical reactions are either absent or very small because the free radical, lacking a formal charge, is less subject to the dipolar action of the solvent (See section 2.5). Upon application of the Hammett equation ($\log \frac{k}{k_0} = \rho\sigma$) to the abstraction reactions of atomic chlorine with substituted toluenes,[144,145] a value of ρ (-0.66) is obtained. This small value of ρ thus indicates a small polar effect.

Another phenomenon of polar effects is in the ability of heteroatoms (nitrogen,[146] oxygen,[147], sulphur[147]) to stabilize an incipient radical when partially developed. It undoubtedly involves the delocalization depicted in structure 11.



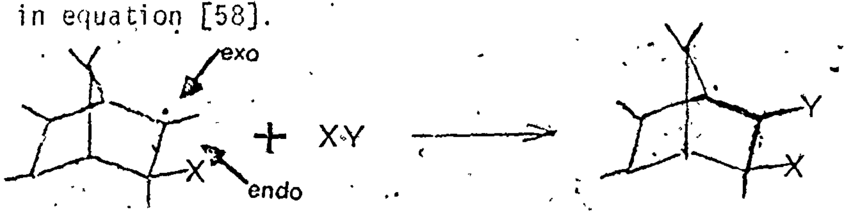
$$\dot{C}-\ddot{X}- \longleftrightarrow \overset{-}{:}C-\overset{+}{\dot{X}}-$$

11

1.6.3 Steric Effects

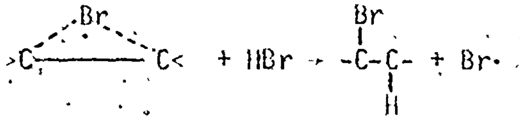
Steric effects have been encountered in a number of free-radical addition reactions. For instance, the stereochemistry of the chain-transfer step in the addition reactions of free radicals to norbornene seems to be governed by the available unhindered solid angle of approach which permits chain transfer readily from the exo side, but not easily from the endo side (cis addition frequently occurs in this case), depicted in equation [58].

[58]



Other steric influences include bridging of olefinic bonds as a rationale for the trans addition observed for such reactions as HBr addition to olefins (equation [59]).

[59].



$$>C\overset{Br}{\overline{\quad\quad}}C< \; + HBr \rightarrow -\underset{}{\overset{Br}{\overset{|}{C}}}-\underset{\underset{H}{|}}{C}- + Br\cdot$$

1.6.4 Solvent Effects

Although in general solvents appear to have little effect on the course of free radical reactions when compared with ionic reactions (See section 2.5), Russell's[148] classical investigation on the complexing of atomic chlorine with basic solvents have shown that under certain circumstances solvent effects can, in fact, become quite profound. Besides, a solvent may affect reactions through one of its physical properties, e.g., polarizability or viscosity (in cage effect studies) alters the rates at which reactions proceed.

Recent investigation[149] of the behaviour of the α-methoxybenzyl radical in a number of solvents shows that solvents possessing donor properties (such as diphenyl ether or diphenyl sulphide) increase the extent of fragmentation of the radical relative to dimerization, while viscous solvents (e.g., hexadecane) favour dimerization.

The effect of solvents capable of forming hydrogen bonds to radicals is usually to lower the reactivity of the radical.[150]

Much less is known of the role played by solvents in the solvation of radicals and of the transition states.[151] The effect of solvents in the solvation and association of radicals is reviewed in a recent article by Martin.[152]

1.7 Kinetic Aspects of Free-Radical Chain Reactions

A radical chain reaction consists of chain initiation, chain propagation, and chain termination reactions. Consider a simple free-radical chain reaction such as that of A_2 with XY as shown in the following sequence (equations [60] to [65]). An example of this type is given by the chlorination of alkanes, where A_2 is the chlorine molecule and XY is the alkane.

Initiation:

[60] $A_2 \xrightarrow{k_1} 2A\cdot$

Propa[illegible]on:

[61] $A\cdot + XY \xrightarrow{k_2} AX + Y\cdot$

[62] $Y\cdot + A_2 \xrightarrow{k_3} AY + A\cdot$

Termination:

[63] $2Y\cdot \xrightarrow{k_4} Y_2$

[64] $A\cdot + Y\cdot \xrightarrow{k_5} AY$

Overall:

[65] $A_2 + XY \rightarrow AX + AY$

The chain length is defined as the number of reaction cycles of the chain carrier before it is destroyed. The chain carriers in the above reaction sequence are A· and Y·. The kinetic aspects of free-radical chain reactions involve an interesting balance of the rates of the initiation and termination steps, as well as the individual radical propagation reactions that comprise the chain sequence itself.

To derive the kinetic rate laws, an assumption is usually applied, called the steady-state approximation. This consists of two parts:

(1) the concentration of the chain carrier, which is very small at all times, remains essentially constant, and

(2) the rate of initiation must be equal to the rate of termination.

We use the above general reaction of A_2 with XY as an illustration, yet for more specific examples, such as the kinetics of polymerization, halogenation and autoxidation, the readers are referred to standard texts such as that by Walling.[1a]

The rate of the overall reaction can be expressed as the rate of either of the two chain-propagating reactions, equations [61] or [62]. Neither of these expressions is particularly useful since both include the concentration of a chain-carrying radical.

$$\text{Rate} = \frac{-d[XY]}{dt} = \frac{d[AX]}{dt} = k_2[A\cdot][XY]$$

or

$$\text{Rate} = \frac{-d[A_2]}{dt} = \frac{d[AY]}{dt} = k_3[A_2][Y\cdot]$$

However, by using the steady-state approximation, we get

$$\frac{d[A\cdot]}{dt} = -k_2[A\cdot][XY] + k_3[Y\cdot][A_2] = 0 = -\frac{d[Y\cdot]}{dt} \qquad (\overset{*}{*})$$

$$k_1[A_2] = k_4[Y\cdot]^2 + k_5[A\cdot][Y\cdot] \qquad (*)$$

From equation $(\overset{*}{*})$, we get

$$k_2[A\cdot][XY] = k_3[Y\cdot][A_2]$$

$$[A\cdot] = \frac{k_3}{k_2}\frac{[A_2]}{[XY]}[Y\cdot] \qquad (**)$$

Substitute (**) into (*), we get

$$k_1[A_2] = k_4[Y\cdot]^2 + k_5\frac{k_3}{k_2}\frac{[A_2]}{[XY]}[Y\cdot]^2$$

$$\therefore \quad [Y\cdot] = \sqrt{\frac{k_1[A_2]}{k_4 + k_5\frac{k_3}{k_2}\frac{[A_2]}{[XY]}}}$$ taking the positive roots

hence the rate of overall reaction is

$$\text{Rate} = \frac{d[AY]}{dt} = k_3[A_2]\sqrt{\frac{k_1[A_2]}{k_4 + k_5\frac{k_3}{k_2}\frac{[A_2]}{[XY]}}}$$

The rate law derived above also depends on the assumption that the chain length is long enough so that the contribution to the rate law from the initiation reaction is negligible. Two limiting cases are (i) if equation [63] is the termination reaction, then the rate will be of three-halves order in $[A_2]$ and independent of $[XY]$.

$$\text{Rate} = k_3[A_2]\sqrt{\frac{k_1[A_2]}{k_4}} = K[A_2]^{3/2}$$

where

$$K = \left(\frac{k_3^2 k_1}{k_4}\right)^{1/2}$$

(ii) If equation [64] is the termination reaction, then the overall order will still be three-halves with the first in A_2 and half in $[XY]$:

$$\text{Rate} = k_3[A_2]\sqrt{\frac{k_1k_2[XY]}{k_3k_5}} = K'[A_2][XY]^{1/2}$$

where

$$K' = \left(\frac{k_1k_2k_3}{k_5}\right)^{1/2}$$

The kinetic chain length can be defined as the rate of one of the propagation reactions (R_p) divided by the rate of termination reaction (R_t).

$$\text{Kinetic chain length} = \frac{R_p}{R_t} = \frac{k_3[Y\cdot][A_2]}{k_4[Y\cdot]^2}$$

$$= \frac{k_3}{k_4}\frac{[A_2]}{[Y\cdot]}$$

It is evident that the kinetic chain length is inversely proportional to the concentration of the chain-carrying radical.

1.8 Bond Dissociation Energies

Bond dissociation energies are of critical importance in radical chemistry. Whether or not a reaction is exothermic or endothermic is meaningful to us; a very endothermic process cannot be a propagation step in a radical chain reaction. Consider a reaction between a radical R· and a substrate AB, ΔH is given by the difference in the dissociation energies of the R-A and A-B bonds. The value of ΔH will determine whether the reaction will take place, if the entropy component, TΔS, is small. Therefore, to predict approximately the relative stability of radicals and the relative energies of radical reactions, data of bond dissociation energies will be required.

The bond dissociation energy is defined as the heat of reaction on homolysis of the species concerned and for a species X-Y is denoted by D(X-Y) (equation [66])

[66] $X\text{-}Y \rightleftharpoons X\cdot + Y\cdot \qquad \Delta H = D(X\text{-}Y)$

By this definition $D(X-Y)$ is also the activation energy E_a for the above reaction assuming that the reverse reaction proceeds with little or no activation energy.

The methods for determining bond dissociation energies will not be mentioned here; the reader is referred to several review articles by Kerr[153] or Benson.[154,155] Numerous data on bond dissociation energies can also be found in those articles.

1.9 Catalysis in Free-Radical Chain Reactions

Although catalysis is a common phenomenon encountered in various aspects of chemistry, yet there are only scattered observations of catalysis in radical chain reactions. We do not consider initiators as catalysts, although many people still use the term 'catalysis' loosely in the literature by saying that "the reaction is catalysed by an initiator". In all cases, the initiator is destroyed and unrecovered at the end of the reaction, so the definition of catalysis is, in fact, violated.

One earlier example of catalysis was provided by Waters,[156,157] who used thiols to catalyse the AIBN-initiated decarbonylation of aldehydes. They found that the amount of CO evolved was never more than that of N_2 formed from the azo compound (dimethyl-2,2'-azoisobutyrate). However, the addition of as little as 0.5 mole % of the thiol to the mixture increased the extent of aldehyde decomposition, as measured by CO evolution, to 80-90% for α-branched aldehyde such as 2-ethylhexanal. This catalysis involves a thiyl radical acting to abstract the aldehydic hydrogen atom, and after the resulting RĊO radical loses CO, a hydrogen atom is donated from the thiol to the R· radical, and the R'S· is regenerated. Hence, the chain sequence is given in equations [67] to [70].

[67] $Me_2\dot{C}CO_2CH_3 + R'SH \rightarrow R'S\cdot + Me_2CHCO_2CH_3$

[68] $R'S\cdot + RCHO \rightarrow R'SH + R\dot{C}O$

[69] $R\dot{C}O \rightarrow R\cdot + CO$

[70] $R\cdot + R'SH \rightarrow RH + R'S\cdot$

They had noticed that very low concentrations of thiol noticeably enhanced the extent of CO evolution, and as the thiol concentration was increased the percentage yield reached a high value which varied little over a 10-20 fold change of thiol content, though it dropped appreciably before the amount of thiol became chemically equivalent to the amount of azo compound used to generate the primary free radicals.

There would be three alternative chain endings (equations [71], [72] and [73]) depending on the thiol concentrations.

[71] $2R'S\cdot \rightarrow R'SSR'$

[72] $R\cdot + R'S\cdot \rightarrow RSR'$

[73] $(CH_3)_2\dot{C}CO_2CH_3 + R'S\cdot \rightarrow (CH_3)_2CCO_2CH_3SR'$

Another example is provided by the use of thiols to catalyze the exchange of hydrogens between organic substrates. There are many examples of such catalysis (recently reviewed by Kellogg[158]), but perhaps the following is the most dramatic.[159] When benzhydryl radicals were produced in diphenylmethane solvent which was labelled with carbon-14, the exchange represented by equation [73] was slow relative to the termination (equation [74]) and no radioactivity was found in the dimer product. However, when 0.04 M thiophenol was added to the solution, 17% exchange was found and the yield of dimer was reduced. Thus, it was clear that [75] and [76] were faster than [73]. Furthermore, the reduced yield of dimer indicated that a considerable fraction of the termination was diverted to [77].

[72] $Ph_2CH\text{-}N{=}N\text{-}CHPh_2 \xrightarrow{60°} 2Ph_2CH\cdot$

[73] $Ph_2\dot{C}H + Ph_2CH_2^{*} \xrightarrow{slow} Ph_2CH_2 + Ph_2\dot{C}H^{*}$

[74] $2Ph_2\dot{C}H \rightarrow Ph_2CHCHPh_2$

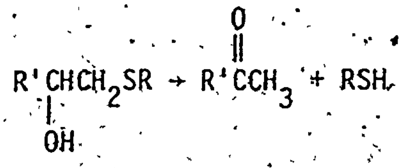
[75] $Ph_2\dot{C}H + PhSH \rightarrow Ph_2CH_2 + PhS\cdot$

[76] $PhS\cdot + Ph_2CH_2^{*} \rightarrow PhSH + Ph_2\dot{C}H^{*}$

[77] $2PhS\cdot \rightarrow PhSSPh$

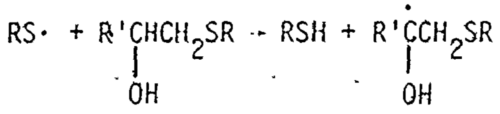
Hydrogen bromide has been used to catalyse radical addition of thiols to olefins.[160] The addition of thiyl radicals to olefins is reversible; and this reversibility can be suppressed by the use of a particular active hydrogen donor like HBr as a chain transfer agent.

Huyser and Kellogg[161] have demonstrated the use of thiols to catalyze the reaction represented by equation [78].

[78]


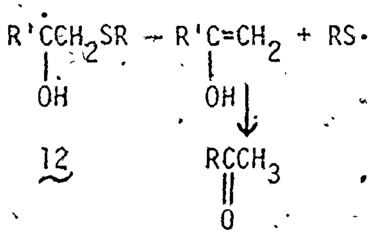
$$R'\underset{\substack{|\\OH}}{C}HCH_2SR \rightarrow R'\overset{\substack{O\\\|}}{C}CH_3 + RSH$$

A radical chain mechanism was proposed in which abstraction of a hydrogen atom by RS· is followed by a rapid cleavage of radical 12; this forms another RS· and the enol of the ketone, which subsequently ketonizes (equations [79] and [80]).

[79] 

$$RS\cdot + R'\underset{OH}{\underset{|}{C}}HCH_2SR \rightarrow RSH + R'\underset{OH}{\underset{|}{\dot{C}}}CH_2SR$$

12

[80] 

$$R'\underset{OH}{\underset{|}{\dot{C}}}CH_2SR \rightarrow R'\underset{OH}{\underset{|}{C}}{=}CH_2 + RS\cdot \quad \downarrow \quad R\overset{}{\underset{O}{\underset{\|}{C}}}CH_3$$

12

Catalytic processes involving oxidation-reduction reactions by transition metal ions, have been reviewed by Kochi.[162,163]

CHAPTER 2

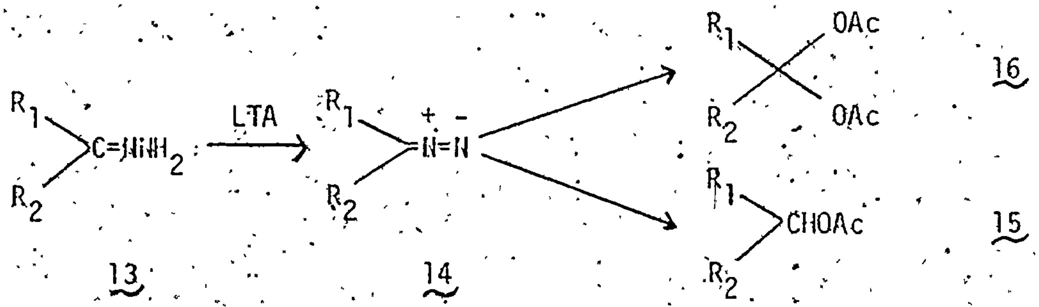
REACTIONS OF LEAD TETRAACETATE WITH KETONE HYDRAZONES

Lead tetraacetate (LTA) has been widely used as a reagent throughout organic chemistry for almost fifty-six years.[164] It is a very versatile reagent and it reacts with a variety of compounds such as 1,2-glycols,[165] sugars,[166] sterols,[167] oximes,[168] alcohols,[169] semicarbazones,[170,171] hydrazones,[172] azomethines,[173] azines[174] and many other organic nitrogen compounds.[175] A review of the oxidative cyclization of derivatives of carbonyl compounds with a number of oxidizing agents including LTA has been published.[176] In this chapter, the discussion will be mainly on the reactions of LTA with ketone hydrazones.

2.1 Unsubstituted Hydrazones

N-Unsubstituted hydrazones 13 are dehydrogenated to the corresponding diazocompounds 14,[177,178] depicted below (equation [81]).

[81]

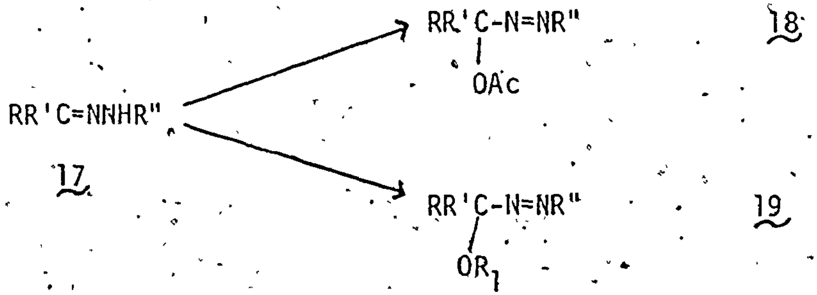


Only the more stable bis(trifluoromethyl)-,[179,180] dicyano-,[181] and diphenyl-diazomethane[182] derivatives have been isolated. In general, the reaction products are substituted monoacetoxy alkanes 15 or diacetoxy alkanes 16 resulting from further reactions of the intermediates 14.[177,178] With alicyclic hydrazones rapid reactions are observed and olefins are formed along with the acetoxylated products.[177,183]

2.2 Monosubstituted Hydrazones

In general, ketone hydrazones 17 upon LTA oxidation, yield azo-acetates 18 in CH_2Cl_2 or azoether 19 in alcohol medium, according to equation [82].

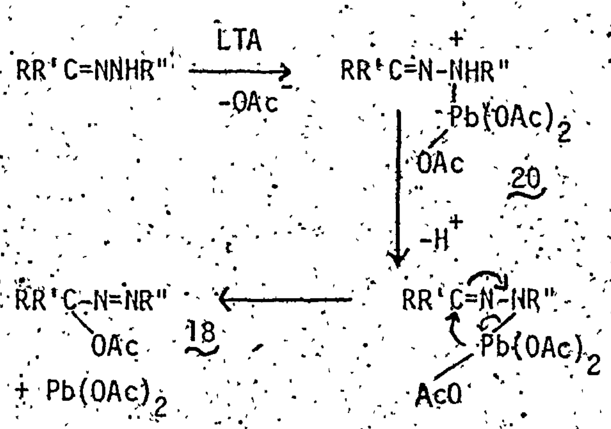
[82]



RR'C=NNHR"
17
RR'C-N=NR"
OAc
18
RR'C-N=NR"
OR_1
19

The isolation of azoacetates 18 was first reported by Iffland.[184] A free-radical mechanism was proposed by him, and more recently by Gillis[174] to explain the reaction with ketone hydrazones. Although free radicals are detected by e.s.r. during the oxidation of oximes,[185] there is no such intermediate in the reaction with substituted hydrazones.[186] The rates of these reactions were found to be more rapid in polar solvents suggesting a polar mechanism[186] (Scheme II). Reactions

Scheme II

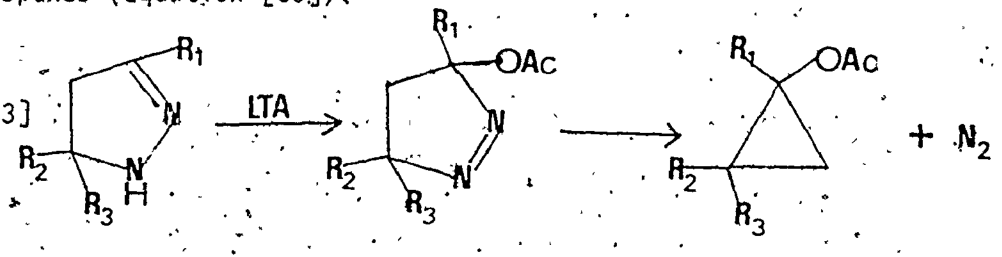


RR'C=NNHR"
LTA
-OAc⁻
RR'C=N-NHR"
+
$Pb(OAc)_2$
OAc
20
$-H^+$
RR'C=N-NR"
$Pb(OAc)_2$
AcO
RR'C-N=NR"
OAc
18
$+ Pb(OAc)_2$

carried out in alcoholic solvents yield azoethers 19 which arise by an intermolecular displacement of the lead salt in 20 and not by exchange with azoacetates.[186]

A wide range of azoacetates 18 has been prepared[174,184,186-194]. The azoacetates are useful intermediates for further synthesis. Azoacetates are readily cyclized in the presence of Lewis acids to indazoles.[195] Freeman[194] has developed a new route to substituted cyclopropanes (equation [83]).

[83]

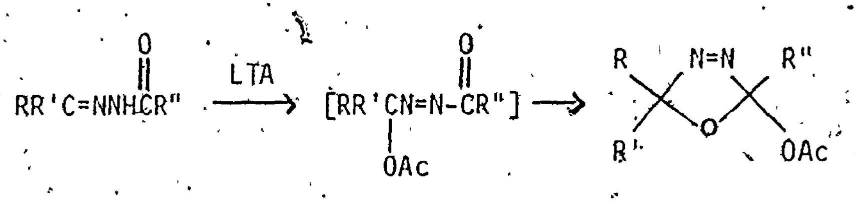


Bhati[190,196] has studied the reactions of LTA with benzenesulphonyl- and toluenesulphonyl-hydrazones of acetone, cyclohexanone and benzophenone. The parent ketones and nitrogen were obtained as identifiable products. He suggested a direct-oxidation mechanism for the formation of ketone. Later, Norman[189] indicated that an intermediate geminal diacetoxy compound that decomposed to the ketone may have been formed.

The LTA oxidation of benzophenone N-carbethoxyhydrazone was reported[197] to give a complex mixture of products which include benzophenone, the expected azoacetate (28%), and a rearrangement product, 2-oxo-1,1-diphenylpropylethylcarbonate.

Ketone carbonylhydrazones of type 21 readily cyclize on treatment with LTA to Δ^3-1,3,4-oxadiazolines 23 (equation [84]).

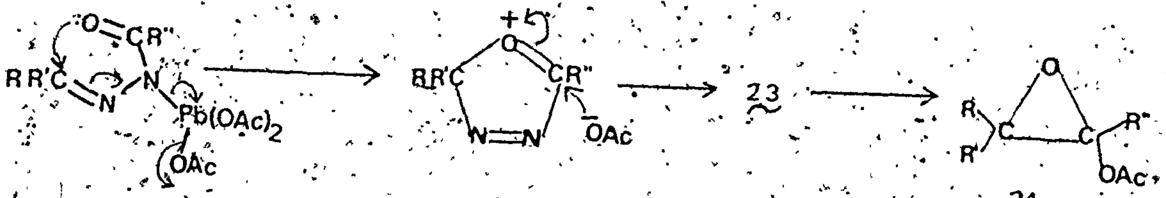
[84]



21 22 23

This cyclization (equation [84]) was first reported by Hoffmann.[198-201] He envisaged an ionic mechanism for the formation of 23. This involves fission of acetate ion from the azoacetate, presumably an intermediate, followed by attack on the resulting carbonium ion by the carbonyl oxygen and subsequently migration of acetate ion to the carbonyl carbon. This cyclization was also observed by Norman.[189] However, he suggested a polar mechanism that does not involve an azoacetate intermediate (equation [85]). Both workers have found that the Δ^3-1,3,4-oxadiazolines 23 lost nitrogen on warming to form the epoxides 24 (equation [85]).

[85]



24

Examples of the cyclization of other types of keto carbonylhydrazones on treatment with LTA can be found in a review article by Warkentin.[176]

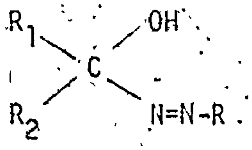
2.3 N,N-Disubstituted Hydrazones

The azoacetates 18 were also formed (up to 75%) from LTA oxidation of N,N-disubstituted hydrazones.[202] This reaction involved a stoichiometry of 2:1 (LTA:hydrazone), in which the first step involved a dealkylation of the hydrazone. The alkyl group cleaved in the reaction was converted to the corresponding aldehyde or ketone. Cleavage of either tert-alkyl or aryl groups was not observed. The mechanism of this reaction of disubstituted hydrazones, however, is not clear.

CHAPTER 3

α-AZOCARBINOLS

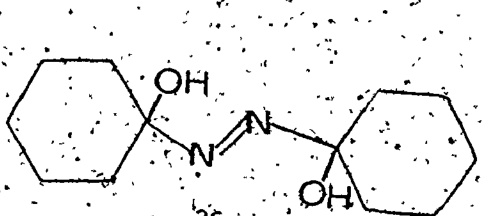
Compounds of the type 25, with an azo linkage and a hydroxy group in geminal juxtaposition, are extremely rare.



25

One reason for the rarity may be due to their thermal instability. Since these compounds may be viewed as adducts of alkyldiimides and carbonyl compounds, it could be assumed that they would decompose readily, with loss of nitrogen to a carbonyl compound and a hydrocarbon. Several names for 25 have been used by different chemists in the literature, such as α-hydroxyazoalkanes, α hydroxyalkyldiazenes, semiaminals of diimide and α-azocarbinols. For convenience sake, the name α-azocarbinols is chosen in the present discussion in referring to compounds of type 25.

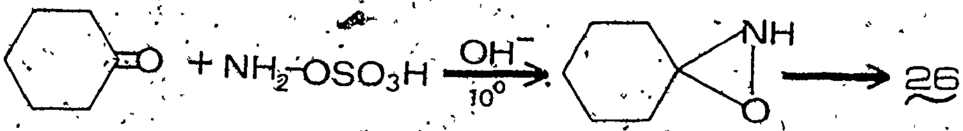
The first α-azocarbinol, 1,1'-dihydroxyazocyclohexane 26, was reported by Schmitz[203,204] in 1963. Compound 26 was obtained as a



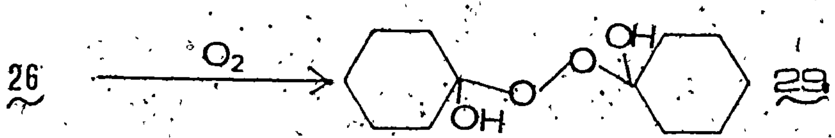
26

crystalline solid upon treatment of hydroxylamine-O-sulfonic acid 27 with cyclohexanone in alkaline solution at 10°C (equation [86]). An iso-oxime of cyclohexanone 28 was suggested as an intermediate in the formation of 26. Compound 26 decomposes readily even at room temperature to cyclohexanone, nitrogen, hydrazine and cyclohexanol as major products. The decomposition mode may involve a radical chain process.[20] At -15°C, compound 26 was stable for several days in the absence of oxygen. However, with air present, 26 was converted to the peroxide 29 in a few days (equation [87]).

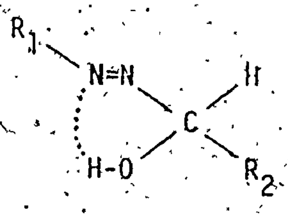
[86]



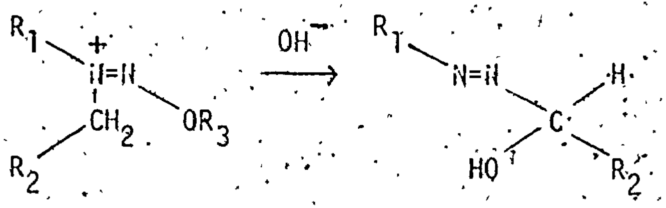
[87]

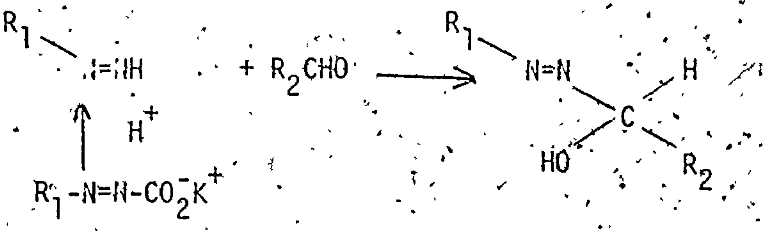


Between 1968 and 1971, Hünig[205-208] reported the synthesis of a series of α-azocarbinols of type 30, via two methods: the action of base on alkoxydiazenium salts (equation [88]), and, more generally, the addition of diazenes to carbonyl compounds (equation [89]).

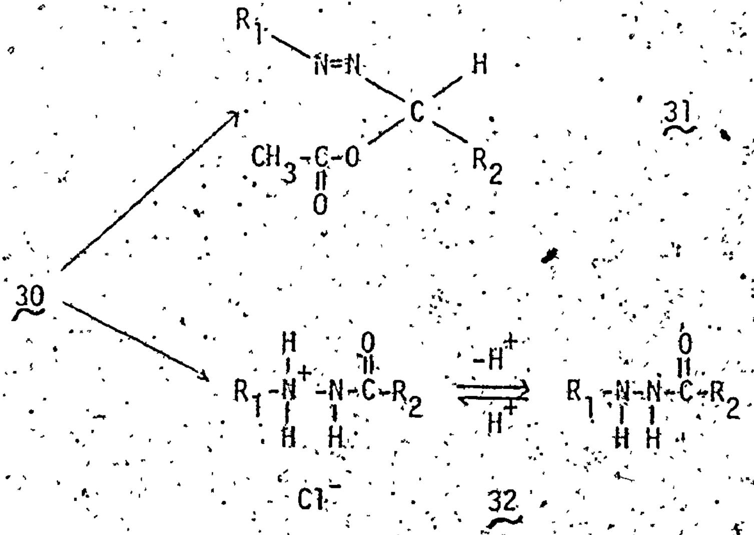


30

[88] 

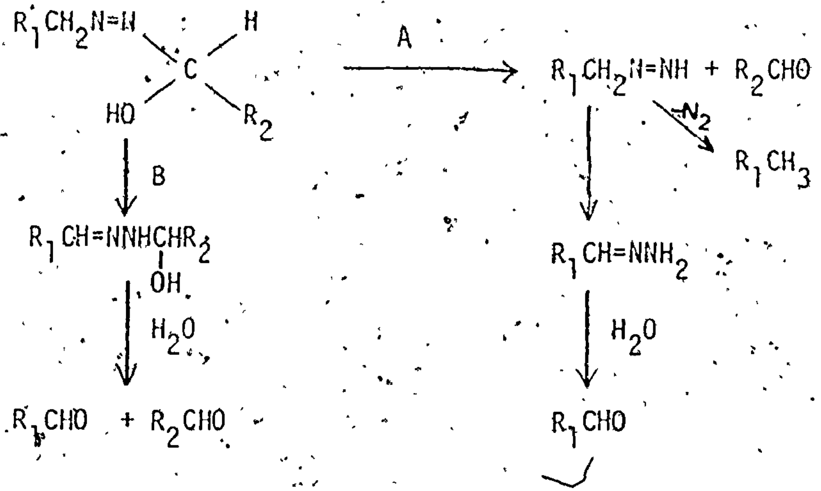
[89] 

Compounds **30** were shown by u.v. and i.r. spectra to possess trans-stereochemistry about the azo bond with intramolecular hydrogen bonding. On esterification by acetic anhydride pyridine mixture, **30** gave the azo-ester **31**, whilst treatment of an ethereal solution of **30** with HCl gas produced the hydrochloride **32** of the isomeric acid hydrazide (equation [90]).

[90] 

Thermolysis of **30** at room temperature gave a mixture of aldehydes. This result was explained as indicated in Scheme III. Path A was considered more likely than path B.

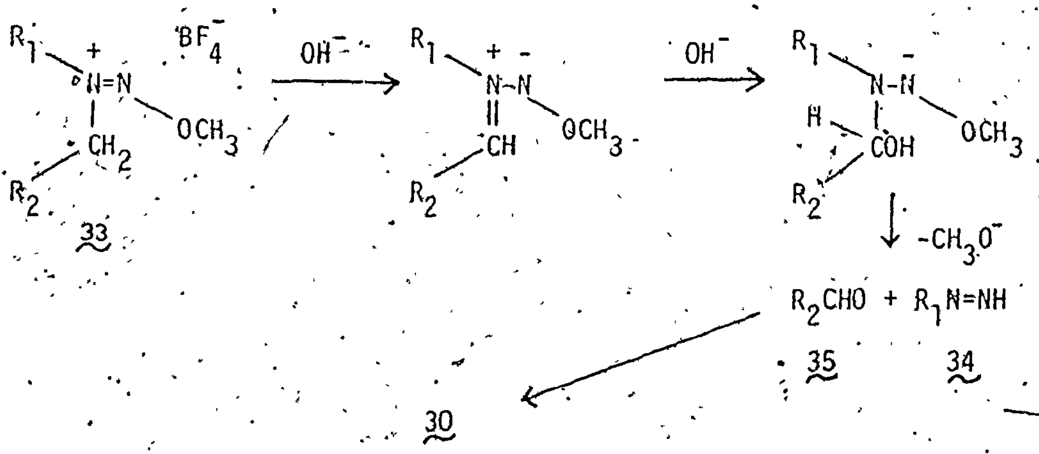
Scheme III



R1CH2N=N
H
C
HO
R2
A
R1CH2N=NH + R2CHO
-N2
R1CH3
B
R1CH=NNHCHR2
OH
R1CH=NNH2
H2O
H2O
R1CHO + R2CHO
R1CHO

The mechanism of formation of 30 from alkoxydiazenium salts, as suggested by Hünig,[207] is shown in Scheme IV.

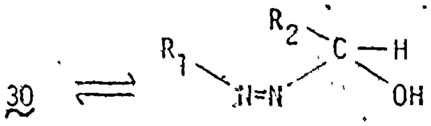
Scheme IV



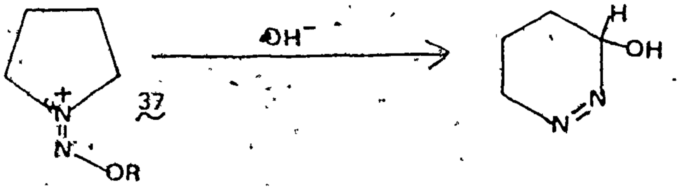
R1
+
N=N
BF4-
CH2
OCH3
R2
33
OH-
R1
+ -
N-N
CH
OCH3
R2
OH-
R1
-
N-N
H
COH
OCH3
R2
-CH3O-
R2CHO + R1N=NH
35
34
30

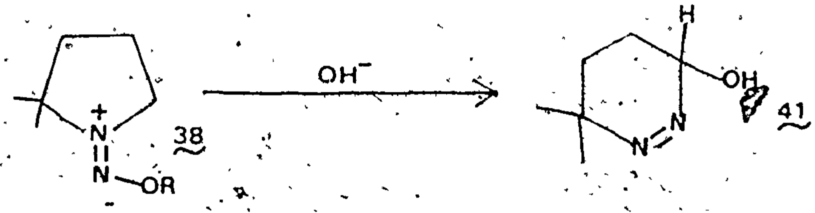
They claimed that 33, on treatment with base, rearranged to the free alkyldiazene 34 and the aldehyde 35. The existence of free diazenes was supported by the formation of 30 from reaction of aldehydes with alkyldiazenes liberated from azocarboxylic acids (equation [89]). Introduction of either a new aldehyde or a different dialkyldiazene into the reaction mixture resulted in its incorporation into the product 30. This observation provided further evidence supporting the mechanistic route in Scheme IV.

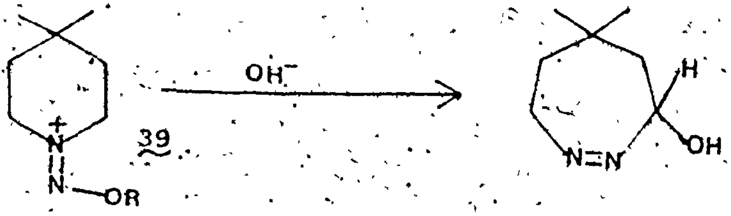
Compounds 30 were shown to possess trans-stereochemistry about the azo-double bond. The non-isolable cis-isomer 36 can only be observed in solution by irradiation of the trans isomer 30 (equation [91]).

[91]

36

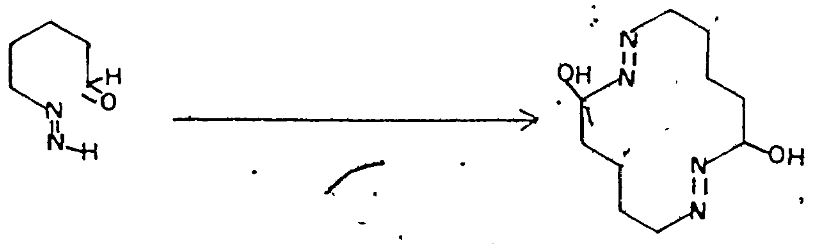
On the other hand, cyclic alkyoxydiazenium salts 37, 38 and 39 give cis-α-azocarbinols 40, 41 and 42, respectively (which were also not isolated) directly on treatment with hydroxide ion (equations [92] to [94]).

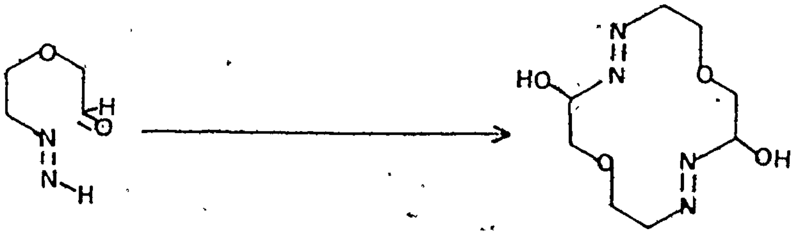
[92]

37 40

[93]

38 41

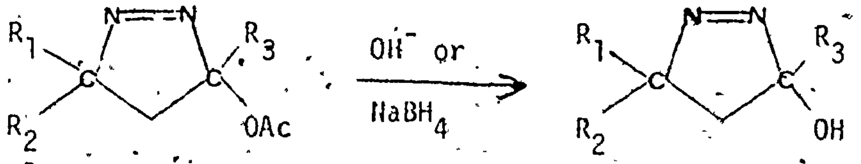
[94]

39 42

Certain cis-azocarbinols with seven-membered rings dimerized amazingly easily to 14-membered rings 42 and 43 with trans-azo double bonds (equations [95] and [96]). The structure of these rings with their unusual functional groups has been established.[208,209]

[95]

42

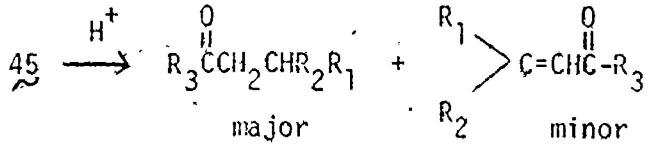
[96]

43

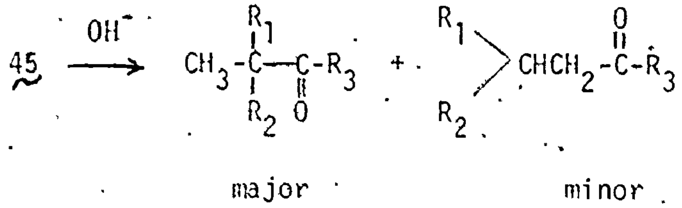
In 1969, Freeman[210,211] reported the preparation of a variety of stable (kinetically) α-azocarbinols (45, 3-hydroxy-3,5,5-trimethylpyrazolines) either by controlled hydrolysis or by hydrogenolysis with sodium borohydride of 44 (3-acetoxy-Δ^1-pyrazolines), equation [97].

[97]


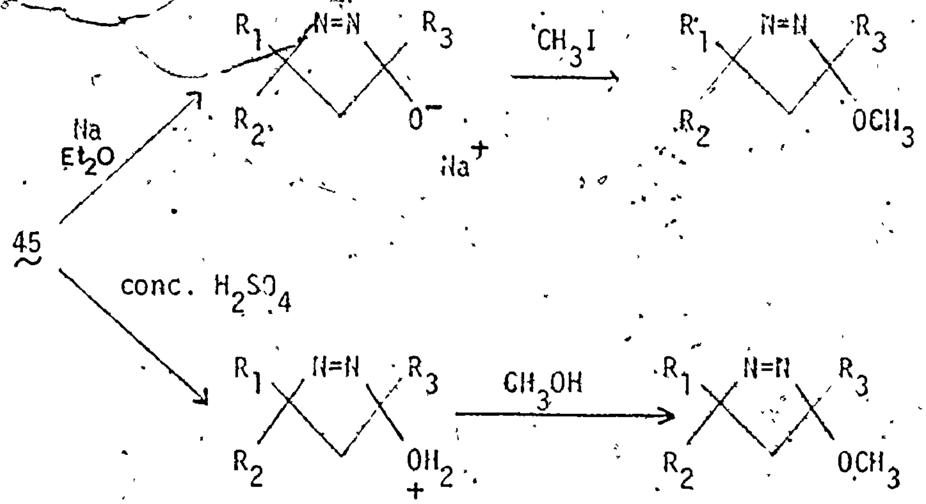
44
45

These α-azocarbinols undergo both acid- and base-catalysed ring opening to give ketones. The acid reactions produce both saturated and unsaturated ketones (equation [98]) while the base reactions yield only saturated ketones but principally those of rearranged carbon skeleton (equation [99]).

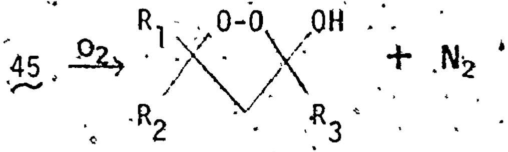
[98]

45
H+
R3CCH2CHR2R1
major
R1
R2
C=CHC-R3
minor

[99]

45
OH-
CH3-C-C-R3
R1
R2
major
CHCH2-C-R3
minor

Esterification of α-azocarbinols 45 to 3,5-dinitrobenzoates was also reported. Also, 45 may be etherified under closely controlled conditions (equation [100]).

[100]

45
Na
Et2O
R1
N=N
R3
R2
O-
Na+
CH3I
OCH3
conc. H2SO4
OH2
+
CH3OH

Compounds 45 were found to be quite thermally stable, and could be kept at low temperature for long periods without appreciable decomposition. However, after several weeks in air at room temperature, 45 was transformed in high yield to a peroxide 46 [212] (equation [101]).

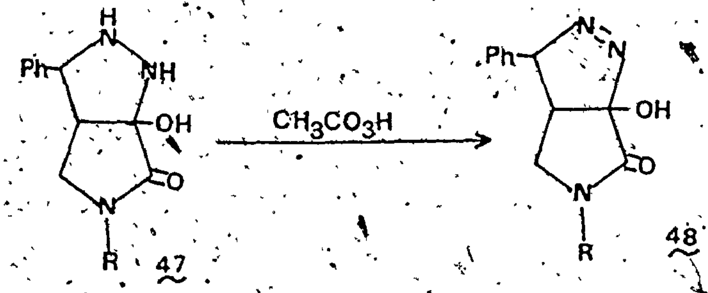
[101]

45
O2
R1
O-O
OH
R2
R3
+ N2

46

With extended heating at high temperatures, 46 decomposed to ketonic products.

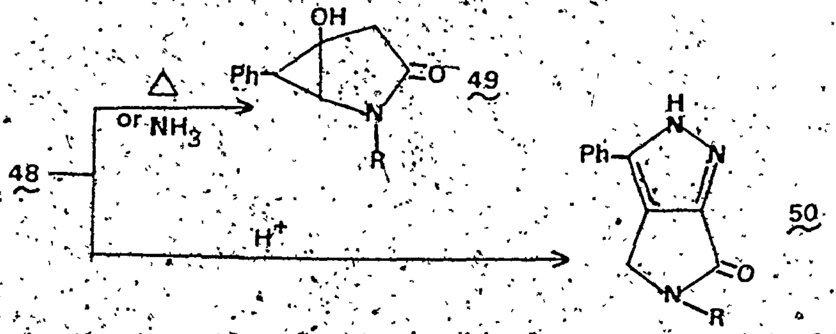
A somewhat more complicated example was reported in 1970 by Southwick[213] wherein the oxidation of the α-hydroxyhydrazines 47 yield the azocarbinols 48 (equation [102]).

[102]



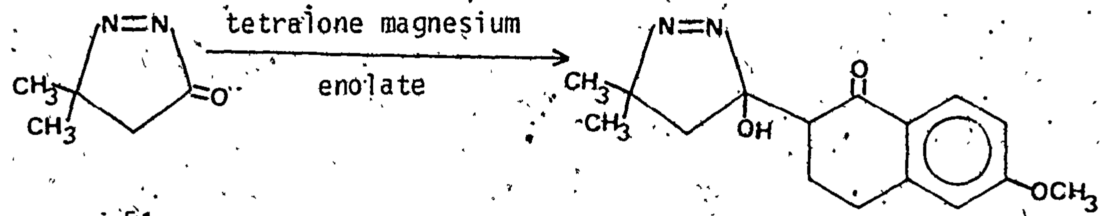
The presence of the cis-azo linkage in 48 was shown by infrared absorption at 6.45 μ[214] and ultraviolet absorption at 342 mμ. Compounds 48 gave typical pyrazoline reactions: thermal decomposition to cyclopropanols 49 and acid-catalysed dehydration to pyrazoles 50 (equation [103]).

[103]



Another example of an azocarbinol was reported in 1970 by Nagator and Kamata.[215] They synthesized 2-(5,5-dimethyl-3-hydroxy-1-pyrazolin-3-yl)-6-methoxy-1-tetralone, 51, by the reaction of 5,5-dimethyl-1-pyrazolin-3-one 52 with the bromomagnesium enolate of 6-methoxy-1-tetralone (equation [104]).

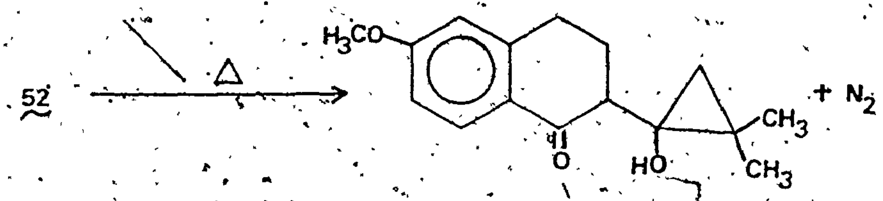
[104]



51 52

Refluxing 52 in 2,4,6-collidine resulted in loss of nitrogen and in the formation of the cyclopropanol derivative 53 (equation [105]).

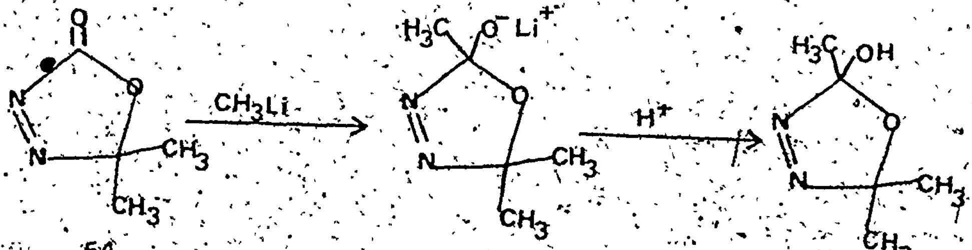
[105]



53

Recently, a new type of azocarbinol 1 was prepared[20,171] in this laboratory, by treatment of 5,5-dimethyl-Δ^3-1,3,4-oxadiazolin-2-one 54 with methyl lithium in ether at 0°, and subsequent hydrolysis, leading to 2-hydroxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline, 1 (equation [106]).

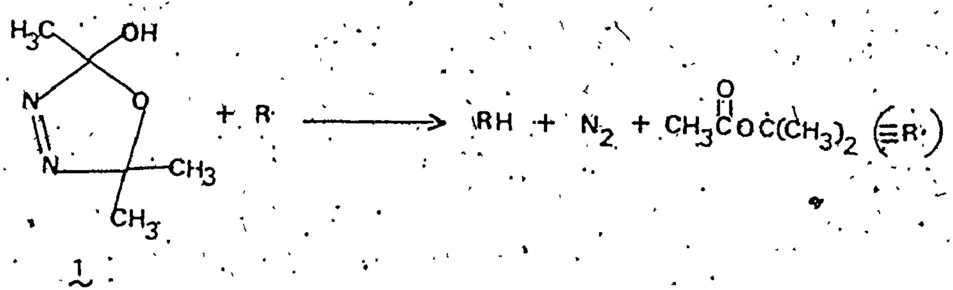
[106]



54 55 1

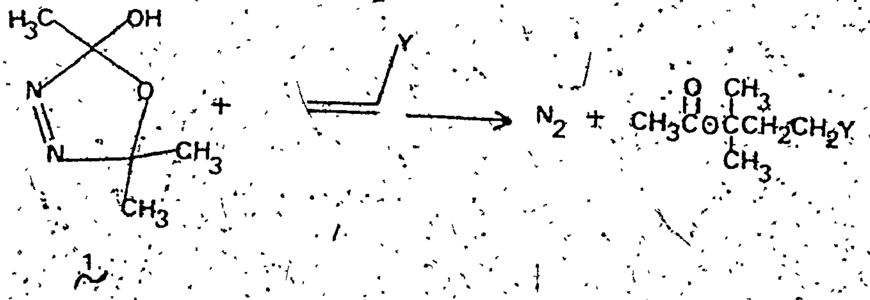
Compound 1 was too unstable to be isolated analytically pure and its structure was established from its spectra and its decomposition products. In benzene solution, 1 decomposed to isopropylacetate nearly quantitatively (equation [107]). The mechanism of its decomposition was confirmed to be a free radical chain process both by radical inhibition with triphenylstannane and by radical spin trapping experiments.

[107]


H3C
OH
N
N
O
CH3
CH3
+ R·
RH + N2 + CH3COC(CH3)2 (≡R·)
O
1

Compound 1 is such a good hydrogen donor that even phenoxy radical from 2,6-di-t-butyl-4-methylphenol can abstract with ease. Such excellent chain transfer ability of 1 makes it a good reagent for radical chain addition yielding small molecules. More than a dozen tertiary acetates were synthesized, via radical chain processes, from the reactions of 1 with unsaturated compounds. The overall addition is shown below (equation [108]).

[108]

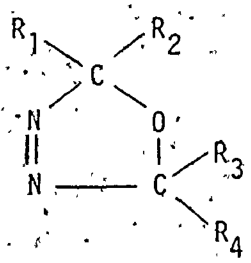

H3C
OH
N
N
O
CH3
CH3
+
Y
N2 + CH3COCCH2CH2Y
O
CH3
CH3
1

CHAPTER 4

DECOMPOSITION OF Δ^3-1,3,4-OXADIAZOLINES

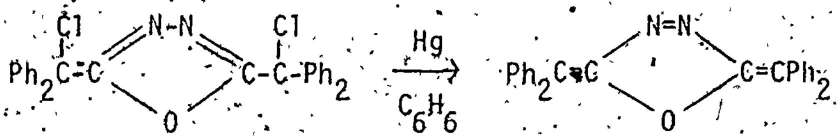
The thermolysis of azo compounds has been reviewed previously (see Section 1.2.1). In this chapter, we only mention the decomposition of Δ^3-1,3,4-oxadiazolines, which can be considered as a specific example of the thermolysis of 5-membered cyclic azo compounds.

The Δ^3-1,3,4-oxadiazoline ring system 56 has been known for almost sixty-five years. The earliest examples, reported in 1911 by



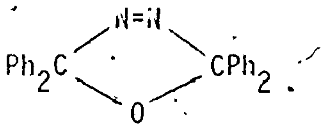
56

Stollé and Laux,[216] were obtained by reactions of mercury with bisdiphenylchloromethylfurodiazole in benzene (equation [109]).

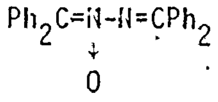
[109]


57

It was observed in 1938 by Schönberg[217] that benzophenone and diphenyldiazomethane were obtained upon thermolysis of 2,2,5,5-tetraphenyl-Δ^3-1,3,4-oxadiazoline 58. The diphenyldiazomethane was also reported to decompose further to benzophenone azine and nitrogen. The compound 58 was obtained by the oxidation of benzophenone oxime with potassium ferricyanide. However, the formation of 58 from the benzophenone oxime oxidation with potassium ferricyanide was disputed by Anwers[218] and Dyer.[219] They both claimed that the product of oxidation was diphenylketazinoxide 59 instead of compound 58.



58



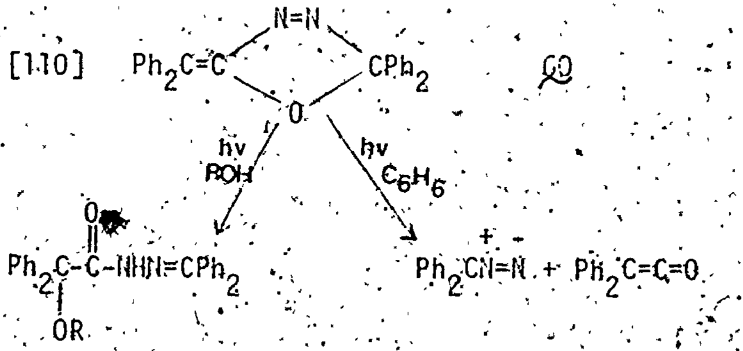
$Ph_2C=N(\rightarrow O)-N=CPh_2$

59

Schönberg[220] published the oxidation of di-p-tolyl ketoxime and p,p'-dimethoxybenzophenone oxime with potassium ferricyanide in 1939. In both cases, the product was claimed to be the 2,2,5,5-tetraaryl-Δ^3-1,3,4-oxadiazoline, supporting his earlier observation.

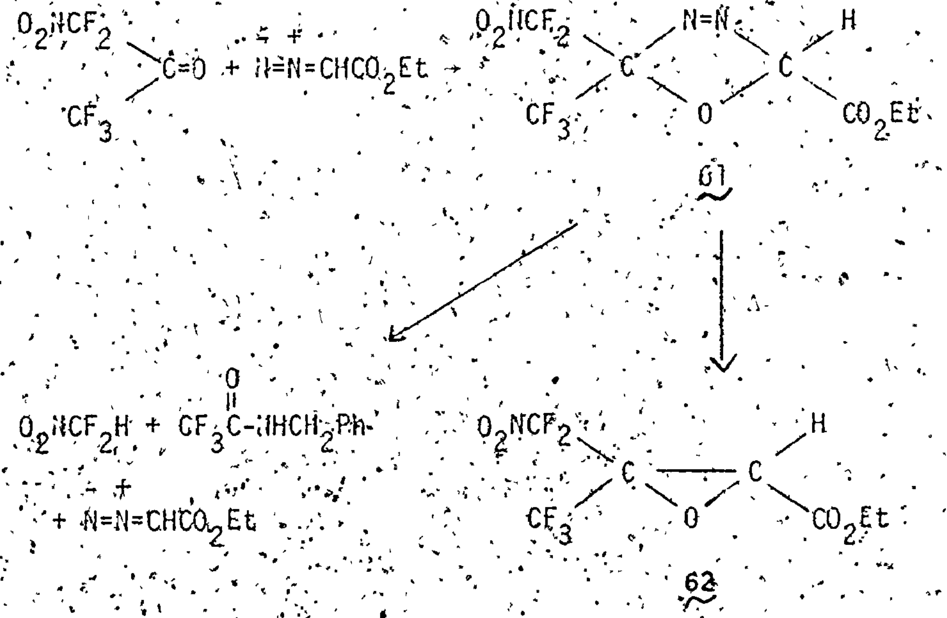
In 1960, Kirmse[221] studied the photolysis of oxadiazolines 57 and 60. Compound 60 was found to be labile to ultraviolet light while 57 was stable. In hydroxyl free solvents such as benzene, 60 decomposed to diphenyldiazomethane and diphenylketene. However, in hydroxylic solvents such as acids or alcohols, addition products were obtained (equation [110]). Mechanisms were not given.

[110]



Michejda[222] reviewed the work of Kirmse in 1968 and suggested a mechanistic scheme to account for the observed results. In 1964, Gambaryan[223] reported the preparation of a fluoro-substituted oxadiazoline 61 from the reaction of ketone with the diazo compound (equation [111]).

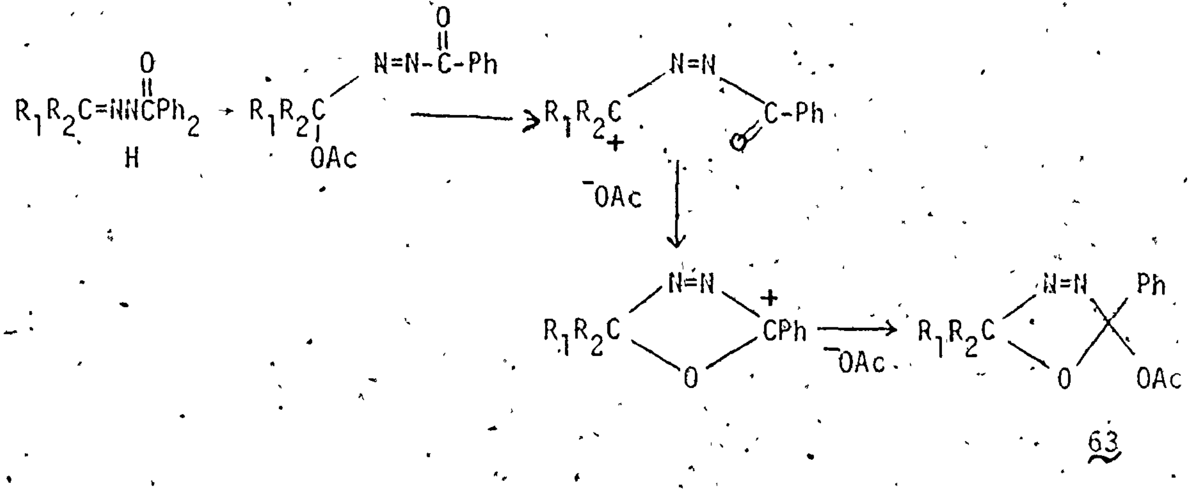
[111]


O_2NCF_2
CF_3
C=O
+ $\bar{N}=\overset{+}{N}=CHCO_2Et$
N=N
H
CO_2Et
O
61
O_2NCF_2H + $CF_3\overset{O}{\overset{\|}{C}}$-NHCH$_2$Ph
+ $\bar{N}=\overset{+}{N}=CHCO_2Et$
62

On thermolysis, 61 gave the epoxide 62. Reaction of 61 with benzylamine yielded difluoronitromethane, N-benzyltrifluoroacetamide and ethyl diazoacetate (equation [111]).

Ketocarbonylhydrazones have been observed to yield Δ^3-1,3,4-oxadiazolines on treatment with LTA (see Section 2.2). Hoffmann[198-201] had discussed the mechanisms of formation as well as subsequent reactions of oxadiazolines from ketone benzoylhydrazones with LTA. An ionic mechanism was proposed which involves fission of acetate ion from the azoacetate followed by attack on the resulting carbonium ion by the carbonyl oxygen and subsequent migration of acetate ion to the carbonyl carbon (equation [112]).

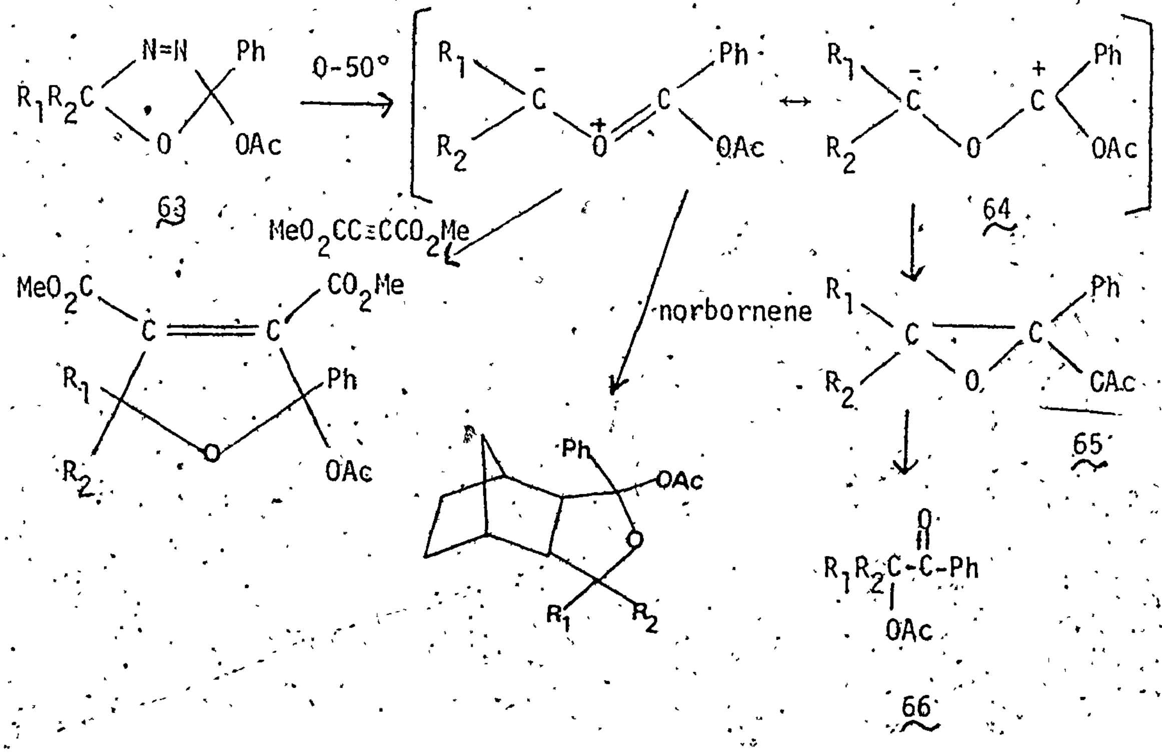
[112]


R1R2C=NNHCPh2
R1R2C(OAc)N=N-C(O)-Ph
R1R2C+
N=N
C-Ph
-OAc
+
CPh
63

However, Norman[189] suggested a polar mechanism which does not involve an azoacetate intermediate (equation [85]).

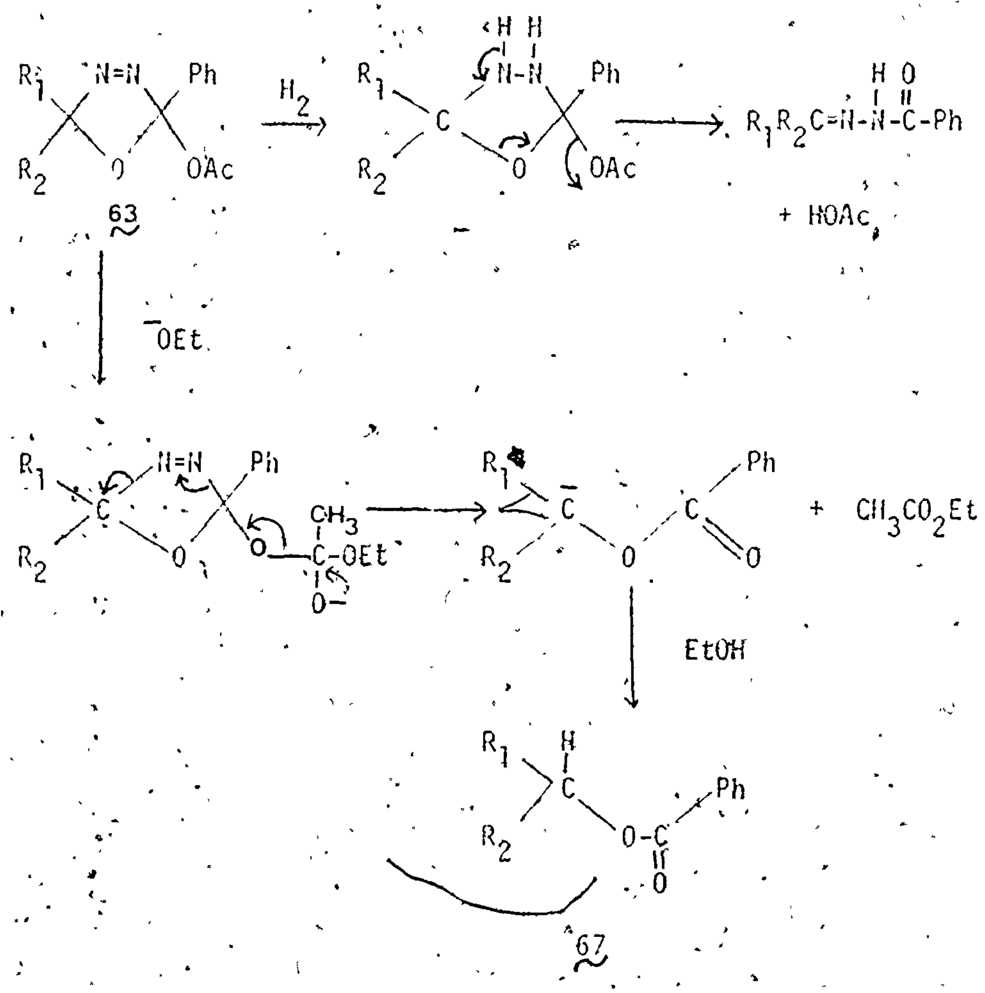
The oxadiazolines 63 were found[189,198-201] to be thermally unstable and decomposed to the epoxyacetates 65 which, on heating, gave the α-acetoxyketones, 66. The decomposition of 63 to 65 was explained by postulating a carbonyl-ylide intermediate 64, formed by loss of nitrogen from 63, which subsequently closed to give 65. The existence of 64 was confirmed by trapping experiments with norbornene and dimethylacetylenedicarboxylate (equation [113]).

[113]


N=N
Ph
OAc
0-50°
63
64
65
66
MeO2CC≡CCO2Me
norbornene
MeO2C
CO2Me
R1
R2
OAc
R1R2C-C(O)-Ph
OAc

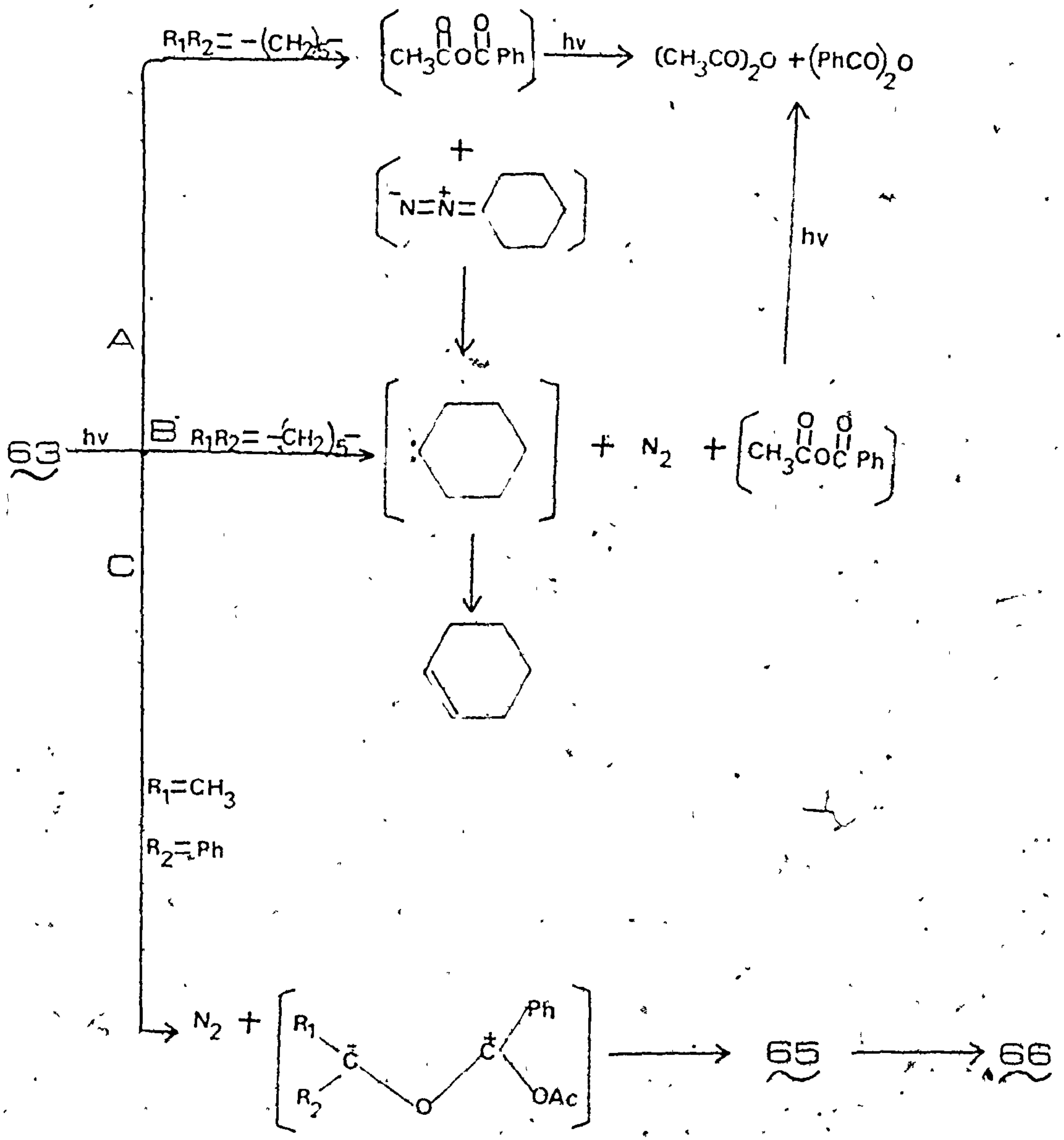
The oxadiazoline 63 was hydrogenated giving the original hydrazone (equation [114]). Treatment of 63 with sodium ethoxide led to the ester 67 (equation [114]).

[114]


R1
N=N
Ph
R2
O
OAc
63
H2
H H
N-N
C
R1R2C=N-N-C-Ph
H O
+ HOAc
OEt
CH3
C-OEt
O−
+ CH3CO2Et
EtOH
67

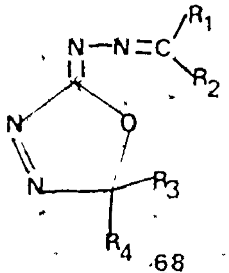
The photolysis of 63 was also studied. The mechanisms of the photolytic reactions were proposed to be dependent on the substituents R_1 and R_2, in Scheme V. When $R_1 = CH_3$, $R_2 = C_6H_5$, the photolysis products were nitrogen, the epoxide 65, and the α-acetoxy ketone 66 (path C). When $R_1R_2 = -(CH_2)_5-$, the products were cyclohexene, nitrogen and a mixture of acetic and benzoic anhydrides (path A or B).

Scheme V

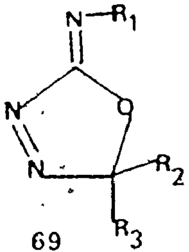

63
hv
A
B
C
R1R2= -(CH2)5-
R1R2= -(CH2)5-
hv
(CH3CO)2O + (PhCO)2O
hv
+
N2
R1=CH3
R2=Ph
N2 +
R1
R2
Ph
OAc
65
66

In 1967, Rajagopalan and Advani[224] reported the 1,3-cycloaddition reactions of the carbonyl-ylides resulting from the mild thermolysis of the oxadiazolines 63. Using N-phenylmaleimide and dimethylacetylenedicarboxylate as traps, they succeeded in isolating adducts similar to those reported by Hoffmann.[198-201]

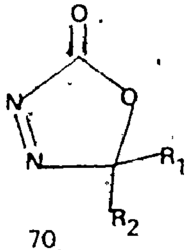
Previous workers[170,225-229] in this laboratory have synthesized Δ^3-1,3,4-oxadiazolines of types 68, 69 and 70, either by the oxidation of ketocarbohydrazones or semicarbazones with LTA.


N—N=C
R1
R2
N
N
O
R3
R4

68


N—R1
N
N
O
R2
R3

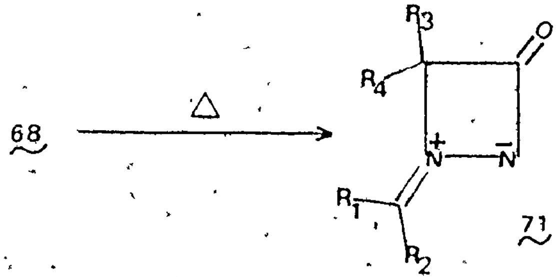
69



70

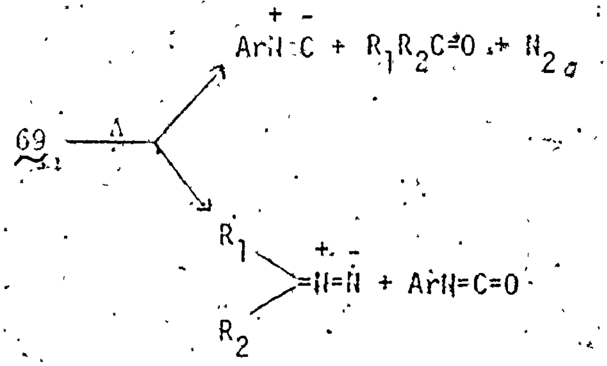
Thermal decomposition of oxadiazolines 68 involves loss of nitrogen to form a four-membered azomethine imine ylid 71,[226-228] (equation [115]).

[115]


68
Δ
R3
R4
O
N
N
R1
R2
71

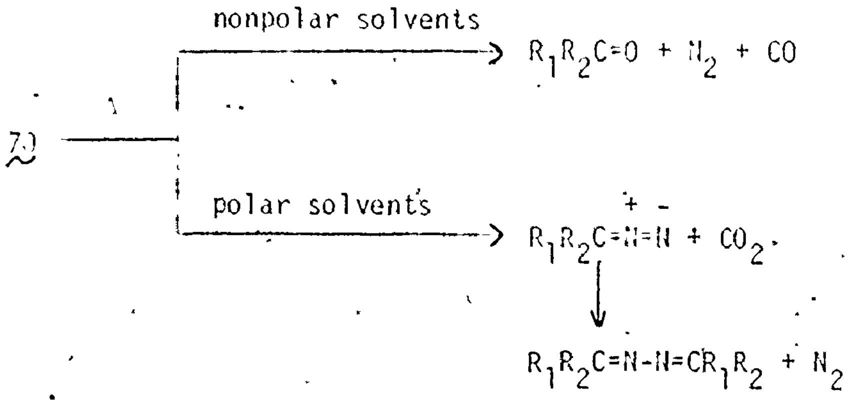
Thermolysis of oxadiazolines 69 gave products arising from two modes of decomposition[170,225] (equation [116]).

[116]


69
Δ
ArN≡C + R1R2C=O + N2
R1
R2
=N=N + ArN=C=O

Pyrolysis of oxadiazolines 70 proceeded predominantly via one of two mechanistic routes, depending on the solvent used[229] (equation [117]).

[117]


70
nonpolar solvents
$R_1R_2C=O + N_2 + CO$
polar solvents
$R_1R_2\overset{+}{C}=N=\overset{-}{N} + CO_2$
$R_1R_2C=N-N=CR_1R_2 + N_2$

CHAPTER 5

RESULTS AND DISCUSSION

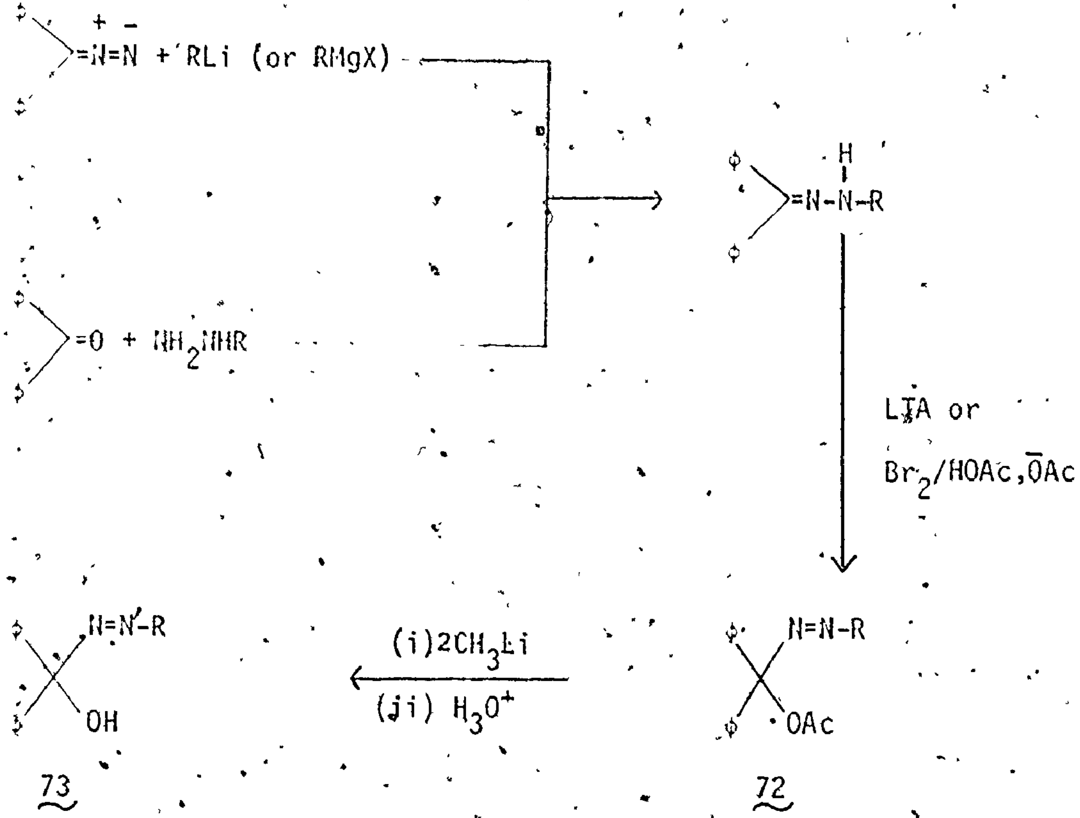
5.1 Synthesis of α-Azodiphenylcarbinols

α-Azodiphenylcarbinols 73 were synthesized according to Scheme VI. The first step involves the preparation of benzophenone N-monosubstituted hydrazones, either by direct condensation of benzophenone with corresponding substituted hydrazines or by the reported reactions of alkyl lithium or Grignard reagents with diphenyldiazomethane.[230,231] The results are collected in Table 1 together with their spectroscopic data. In many cases, the hydrazones prepared were used immediately for subsequent reactions (i.e., bromine or LTA oxidations) without prior purification. Yields of the products were of the order 65-90%. The structures of these compounds were readily established from the appropriate spectroscopic (p.m.r., i.e., m.s.) data (Table 1).

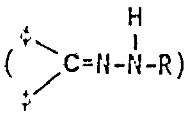
The second step is to convert the hydrazones to azoacetates by oxidations with either bromine or LTA. N-Monosubstituted ketohydrazones 17 are known to yield azoacetates 18 on treatment with LTA (equation [82]). This has been reviewed in Chapter 2 (page 42).

The reaction of bromine with ketohydrazones in acetic acid yielding azoacetates is of importance because this preparative method is comparatively cheap and easier to handle experimentally than the LTA method, although the yields obtained, in general, were lower (Table 2). Two plausible ionic mechanisms can be suggested for this reaction, depicted in Scheme VII.

Scheme VI



+ RLi (or RMgX)
=O + NH$_2$NHR
=N-N-R
LTA or
Br$_2$/HOAc,$\bar{O}$Ac
N=N-R
OAc
(i)2CH$_3$Li
(ii) H$_3$O$^+$
N=N-R
OH
73
72

Table 1: Benzophenone N-Monosubstituted Hydrazones ($(\phi)_2C{=}N{-}\overset{H}{N}{-}R$)

R	p.m.r.	i.r. cm^{-1}	m.s. mol. wt.[a]	M.P. (°C)	Yield
tert-butyl	δ1.18(s,9),δ4.95(broad,s,1) δ7.10-7.53(m,10)	3080,2950,1960,1880,1820,1750,1670,1570,1550,1490,1470,1450,1395,1380,1360,1250,1190,1110,1075,1025,980,915,900,700,692,640.	252(252)	74-75 (lit.^{232} 73.5-75)	77
phenyl	δ3.38(s,1),δ6.72-7.62(m,15)	3345,3090,3060,3030,1960,1880,1820,1770,1600,1500,1450,1340,1315,1300,1250,1190,1175,1125,1105,1070,1030,965,920,885,690,660.	—	137-138 (lit.^{233} 137-139)	82
methyl[b]	δ2.92(s,3),δ4.88(s,1) δ7.00-7.50(m,10)	b	b	41-42(d) (lit.^{230} 42-43)	65
benzyl[b]	δ4.37(s,2),δ5.40(broad,s,1) δ7.00-7.47(m,15)	b	b	78-79(d) (lit.^{189} 77-79)	65
2-hydroxy-ethyl[c]	δ2.75(broad,s,1),δ3.20 (broad,t,2,J=6Hz),δ3.63 (t,2,J=6Hz),δ5.38(broad,s,1),δ7.00-7.50(m,10). The peaks at δ2.75 and δ5.38 disappeared on shaking with D$_2$O.	3450,3280,3010,2800,2700,1950,1870,1800,1750,1650,1480,1450,1440,1320,1180,1125,1070,1050,1030,950,910,690,648.	240(240)	61-62	90
isopropyl[d]	δ1.08(d,6),δ3.12-3.65(m,1) δ4.89(broad,s,1) δ6.93-7.45(m,10)	3275(N-H)	238(238)	—	d

continued......

Table 1 (Continued)

R	p.m.r.	i.r. cm^{-1}	m.s. mol. wt.[a]	M.P. (°C)	Yield %
ethyl[d]	δ1.12(t,3,J=7Hz) δ3.22(q,2,J=7Hz) δ4.92(broad,s,1) δ7.03-7.50(m,10)	3260(N-H)	224(224)	——	d
cyclohexyl[d]	e	3420(NH)	278(278)	——	d
allyl[d]	δ3.87-3.97(m,2) δ4.93-5.07(m,2) δ5.27-5.60(m,1) δ7.20-7.63(m,10)	——	236(236)	——	d

[a] The bracketed number is the calculated molecular weight of the corresponding hydrazone.

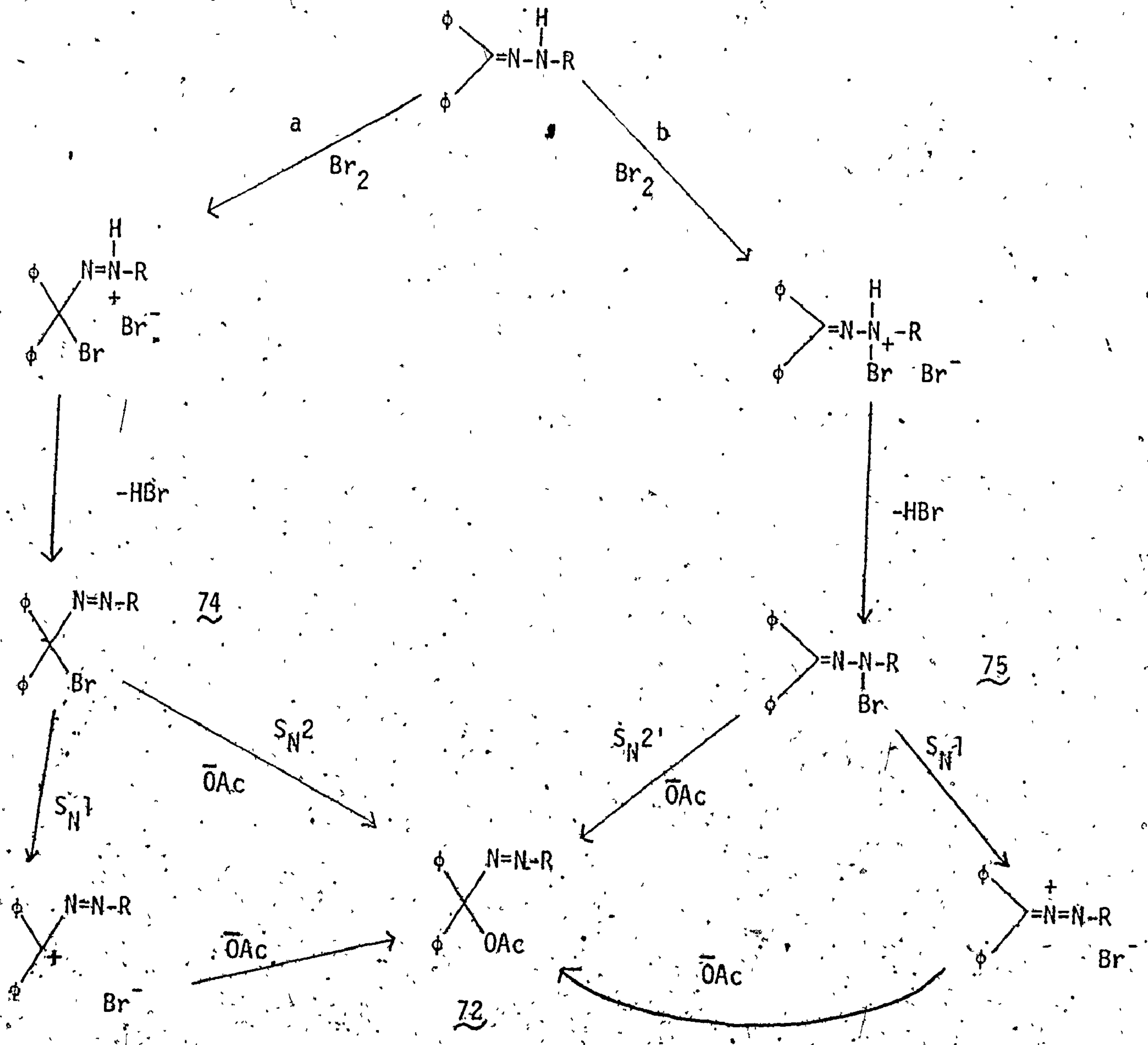
[b] These two compounds decomposed slowly at room temperature with evolution of gas, and their i.r. as well as m.s. spectra were not obtained.

[c] Anal. calcd. for $C_{15}H_{16}N_2O$: C 74.96, H 6.72, N 11.66; found: C 74.44, H 6.67, N 11.97. This compound decomposed slowly in the refrigerator.

[d] These compounds were obtained as crude oils, and no further purification was performed. The yields (by p.m.r.) were of the order 80%.

[e] The system was complex, probably with impurities, and no attempts were made to purify this compound.

Scheme VII

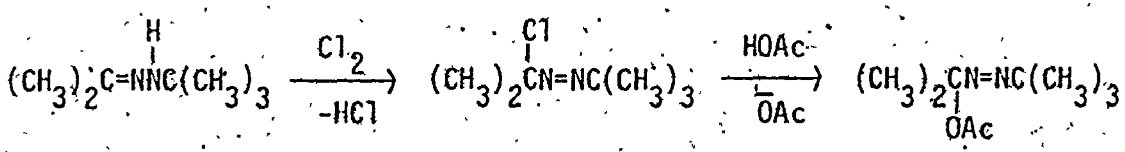

a
Br2
b
Br2
-HBr
-HBr
74
75
SN2
OAc
SN1
SN2'
OAc
SN1
OAc
OAc
72

Path a involves the nucleophilic attack on bromine with anchimeric assistance from the lone pair electrons in the amido nitrogen α- to C=N bond. Following liberation of HBr, compound **74** is formed which yields the azoacetate **72** by either an S_N1 or S_N2 process. The S_N1 process may be more favourable than S_N2 since the site of attack is a bit too hindered for the S_N2 process.

Path b involves the initial attack on bromine by the amido nitrogen, analogous to the postulated attack on lead in LTA oxidation.[189] The product azoacetate **72** is thus formed by resulting attack on compound **75** with acetate ion in either the S_N1 or the S_N2 process.

No reports on the bromination of ketone N-monosubstituted hydrazones appeared in the literature, although the reactions of bromine with aldehyde monosubstituted hydrazones have been extensively investigated by Scott.[234] The only example in close analogy to the present case is the chlorination of tert-butylacetonehydrazone to 2-chloro-2-tert-butylazopropane, followed by solvolysis to 2-acetoxy-2-tert-butylazopropane, recently reported by Malament[235] (equation [118]).

[118]



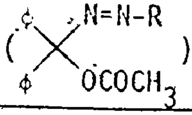
$$(CH_3)_2C{=}N\overset{H}{N}C(CH_3)_3 \xrightarrow[-HCl]{Cl_2} (CH_3)_2\overset{Cl}{C}N{=}NC(CH_3)_3 \xrightarrow[\bar{O}Ac]{HOAc} (CH_3)_2\underset{OAc}{C}N{=}NC(CH_3)_3$$

Based on the results by Malament,[235] path a is more likely than path b as the mechanism for the bromine oxidation of ketohydrazones.

The yields and properties of all the azoacetates prepared are assembled in Table 2. Yields of the products were in the range of 20 to 80%. A singlet peak at δ 2.00-2.10 is present in the p.m.r. spectra of all the azoacetates (Table 2). This peak is due to the protons in the acetate group in the compounds. A strong band near 1760 cm^{-1} is present in the i.r. spectra of all the azoacetates (Table 2), which is due to the stretching of the C=O bond of the acetate. Most of the compounds decompose at their melting points (Table 2).

Norman[189] reported that treatment of benzophenone benzylhydrazone with LTA caused evolution of nitrogen yielding 1,1,2-triphenylethyl acetate (54%) from decomposition of the intermediate azoacetate. However, about 33% pure crystalline benzylazodiphenylmethyl acetate was isolated in the present work. Norman failed to obtain the azoacetate 72 (R = benzyl) most probably because the reaction was not carried out at low temperature. Besides, the solvent (CH_2Cl_2) was removed by distillation, which caused the azoacetate 72 (R = benzyl) to decompose.

Treatment of azoacetates 72 with methyl lithium in ether at -10°C, followed by acidification with NH_4Cl solution, gave α-azodiphenylcarbinols 73 in the final step. Nine such azocarbinols 73 which were prepared are listed in Table 3 together with m.p., spectroscopic data and analyses. Yields were of the order of 70%. The presence of hydroxyl group in these compounds is confirmed by p.m.r. as well as i.r. spectra. The broad singlet peak near δ 5.80, which disappeared on shaking with D_2O, is present in the p.m.r. spectra. The band near 3330 cm^{-1} of medium intensity in the i.r. spectra of all the azocarbinols 73 is attributed to the O-H stretching. Azo (N=N) stretching bands were not observed in the i.r. spectra. However, the Raman spectrum of tert-butylazodiphenylcarbinol 73 (R = t-butyl), taken in the solid state at room temperature, showed N=N stretching at 1587.4 cm^{-1}. The peak at 1650 cm^{-1} (CO of benzophenone) in the i.r. spectra of all the azocarbinols

Table 2: Yields and Properties of Azoacetates 72 ()

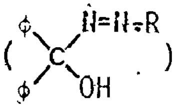
$\phi_2C(N{=}N{-}R)(OCOCH_3)$

R	Yield %	M.P. °C	p.m.r.	i.r. cm^{-1}	Analysis
tert-butyl	70 (LTA) 35 (Bromine)	59-61 (lit.[184] 61-63)	δ1.23(s,9),δ2.08(s,3) δ7.15-7.51(m,10)	3100,3070,3020,2980,2940 1960,1890,1765,1670,1600, 1500,1480,1455,1370,1225, 1195,1185,1090,1025,970, 920,690,650,560.	———
isopropyl	70 (LTA)	69.5-70.5	δ1.21(d,6,J=7Hz),δ2.03(s,3) δ3.87(qe,1,J=7Hz) δ7.08-7.48(m,10)	3100,3070,3040,2980,2940, 1955,1885,1765,1490,1470, 1450,1370,1320,1295,1220, 1195,1185,1110,1085,1040, 1025,970,920,690,660, 625,560.	$C_{18}H_{20}N_2O_2$ Calcd. Fou C:72.93 73. H: 6.81 6. N: 9.46 9.
ethyl	60 (LTA)	77-78	δ1.29(t,3,J=7Hz),δ2.05(s,3) δ4.00(q,2,J=7Hz) δ4.08-7.52(m,10)	3100,3070,3040,2990,2945,1960, 1880,1765,1600,1455,1370,1330, 1295,1230,1200,1190,1090,1050, 1025,965,920,700,675,665.	$C_{17}H_{18}N_2O_2$ Calcd. Fou C:72.30 72. H: 6.43 6. N: 9.93 9.
methyl	45 (LTA)	124-125(d) (lit.[184] 125-126)	δ2.06(s,3),δ2.86(s,3) δ7.13-7.53(m,10)	3050,1750,1480,1450,1360, 1220,1190,1180,1040,1020, 935,915,695.	———
phenyl	80 (LTA) 80 (Bromine)	100-101 (lit.[184] 101-103)	δ2.18(s,3) δ7.20-7.83(m,15)	3650,1950,1850,1750,1480, 1440,1360,1220,1195,1175, 1145,1080,1035,1020,955, 910,695,685.	———
benzyl	33 (LTA)	97-98(d)	δ2.00(s,3),δ4.93(s,2) δ6.87-7.40(m,15)	3100,3075,3040,1955,1870, 1765,1495,1450,1370,1315, 1225,1195,1180,1085,1050, 1020,920,690,675,590.	$C_{22}H_{20}N_2O_2$ Calcd. Fou C:76.71 77. H: 5.85 6: N: 8.14 8.

Continued......

Table 2 (continued)

R	Yield %	M.P. °C	p.m.r.	i.r. cm^{-1}	Analysis
allyl	43 (LTA)	103-104(d)	δ2.03(s,3),δ4.30-4.57(m,2) δ4.93-5.27(m,2) δ5.63-6.17(m,1) δ7.03-7.43(m,10).	3070,3040,1750,1495, 1450,1370,1230,1195, 1185,1110,1085,1045, 1025,925,695.	$C_{18}H_{18}N_2O_2$ Calcd. Foun C:73.43 73.5 H: 6.16 6.1 N: 9.52 9.6
cyclohexyl	20 (LTA)	113-114(d)	δ1.14-1.94(m,10);δ2.04(s,3) δ3.44-3.76(m,1) δ7.06-7.48(m,10)	3070,3040,2950,2900,1950, 1880,1755,1600,1495,1450, 1365,1290,1245,1230,1195, 1180,1135,1085,1035,1025, 970,945,915,865,695,675.	$C_{21}H_{24}N_2O_2$ Calcd. Foun C:74.95 74. H: 7.19 6. N: 8.33 8.
2-hydroxy-ethyl	35 (LTA) 15 (Bromine)	92-93(d)	δ1.93(broad,s,1) δ2.08(s,3) δ3.75-4.25(m,4) δ7.12-7.62(m,10) The peak at δ1.93 disappeared when shaking with D_2O.	3500,3040,3000,2940,2900,2850, 1945,1860,1735,1580,1495,1445, 1420,1360,1230,1190,1180,1110, 1050,1020,950,918,860,695,675.	$C_{17}H_{18}N_2O_3$ Calcd. Fou C:68.42 68. H: 6.08 6. N: 9.40 9.

Table 3: Properties of α-Azocarbinols 73 () $\phi_2C(OH)N{=}N{-}R$

R	M.P. °C	p.m.r.	i.r.[a] cm^{-1}	Analysis
tert-butyl[b]	74-75(d)	δ1.33(s,9),δ5.92(s,1) δ7.28-7.66(m,10) (Taken at -12°C)	3625,3340,2995,1650, 1495,1455,1370,1280, 1325,1280,1195,1070, 1035,945,700	$C_{17}H_{20}N_2O$ Calcd. Found C:76.07 75.88 H: 7.52 7.55 N:10.44 10.30
isopropyl	54-55(d)	δ1.30(d,6,J=7Hz) δ4.03(qe,1,J=7Hz) δ5.63(s,1) δ7.07-7.53(m,10)	3300,3050,2950,2930, 1950,1880,1650,1600, 1450,1360,1320,1280, 1200,1180,1155,1020, 1070,1030 (in $CDCl_3$)	——
ethyl	44-45(d)	δ1.35(t,3,J=7Hz) δ4.05(q,2,J=7Hz) δ5.60(s,1) δ7.03-7.53(m,10)	3330,3050,2960,1650, 1490,1450,1370,1320, 1200,1100,1065,1030, 940,905,700,670,640.	——
methyl	not isolated pure	δ3.73(s,3) δ5.47(s,1) δ6.97-7.70(m,10)	3500,3300,2950,2900, 1650,1600,1450,1370, 1320,1280,1200,1065, 1000,940,915 (in benzene)	——
phenyl	75-76(d)	δ5.83(s,1) δ7.10-7.80(m,15)	3380,3050,1950,1870,1800, 1650,1600,1480,1450,1380, 1310,1210,1185,1160,1100, 1070,1030,940,900,700	$C_{19}H_{16}N_2O$ Calcd. Found C:79.13 79.35 H: 5.60 5.83 N: 9.72 9.64
cyclohexyl	52-53(d)	δ1.24-1.94(m,10) δ3.78(m,1),δ5.82(s,1) δ7.14-7.54(m,10) (Taken at -12°C)	3350,3050,2950,2850, 1650,1600,1490,1450, 1370,1360,1350,1200, 1140,1065,1030,940, 905,700	——

Continued......

Table 3 (continued)

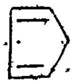
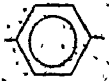
R	M.P. °C	p.m.r.	i.r.^{a} cm^{-1}	Analysis
2-hydroxyethyl	not isolated pure	The spectra of these compounds were complex, and no assignments to the peaks could be made.	3600,3340(OH),1650	———
benzyl	not isolated pure	The spectra of these compounds were complex, and no assignments to the peaks could be made.	3560,3330(OH),1650	———
allyl	not isolated pure	The spectra of these compounds were complex, and no assignments to the peaks could be made.	3300(OH),1650	———

[a] The peak at 1650 cm^{-1} (CO of benzophenone) increased in intensity with time in all cases, as decomposition progressed.

[b] The elemental analysis was performed by A.B. Gygli Microanalysis, Ltd., Toronto.

increased in intensity with time as decomposition progressed.

There are four azocarbinols 73 which could not be isolated in pure crystalline form (Table 3). Their structures were established from their spectroscopic data, spin trapping with nitrosobenzene, reactions with olefins or azobenzene, as well as from their decomposition products in benzene and carbon tetrachloride (see later sections). Elemental analyses were not performed for some crystalline compounds because they are not thermally stable enough to be sent out for analysis. All the azocarbinols thus prepared can be kept at low temperature (about -10°C) for quite a long period.

Attempts to synthesize 73 with R=CH, CH_2CN, $N(CH_3)_2$, , CH_2NO_2, SO_2--NO_2 were not successful.

5.2 Chemistry of α-Azodiphenylcarbinols

5.2.1 Thermal Decomposition

5.2.1.a Decomposition in Carbon Tetrachloride

All the azocarbinols 73 prepared decompose readily at room temperature in carbon tetrachloride yielding benzophenone, chloroform and the corresponding chlorides as the major products. Both the product analysis and the kinetic studies (see below) indicate that the decomposition of 73 is a radical-chain process. A proposed mechanism is depicted in Scheme VIII. The radical R·, generated from 73, abstracts chlorine from CCl_4 giving the alkyl chloride RCl. The resulting trichloromethyl radical, a good chain transfer agent, attacks the hydroxyl hydrogen of 73 thus carrying the chain process. The corresponding compounds RH are not detected; this indicates that the radicals R· abstract chlorine from

CCl_4 much more readily than they abstract H from 73, in dilute solutions of 73 in CCl_4.

The decomposition rate of tert-butyl-α-azodiphenylcarbinol 76 (i.e., 73 with R = t-butyl) was followed by integrating the tert-butyl signals (disappearance of 76 and appearance of tert-butyl chloride) in the p.m.r. spectrum. In each run, the data always give a good fit to the first-order rate law. However, the apparent rate constant was not reproducible even using the same batches of 76 and the same solvent (Table 4). It was also noted that the degassed samples always decomposed much slower than those open to air, but the apparent rate constants were still scattered (Table 4). Therefore, 76 does not undergo the unimolecular fission characteristics of most azo compounds (section, 1.2.1), for which the rate constant is fairly reproducible in different runs under the same conditions. Such non-reproducible rate behaviour means that 76 decomposes via a radical chain process, the rate of which can depend strongly on the concentrations of adventitious initiators and/or inhibitors and/or chain transfer agents.

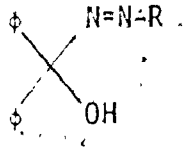
The derivation of the rate law for the mechanism in Scheme VIII is similar to that given in section 1.7 (page 32). Using the steady state approximation, the rate of disappearance of 73 is expressed in equation [119].

$$[119] \quad \text{Rate} = k_3[73]\left(\frac{k_1[73]}{(k_5+k_6)\,\dfrac{k_3^2}{k_2^2}\,\dfrac{[73]^2}{[CCl_4]^2} + \dfrac{k_7k_3}{k_2}\,\dfrac{[73]}{[CCl_4]} + k_8}\right)^{1/2}$$

(if the chain length is long).

Scheme VIII

Initiation:



$$\xrightarrow{k_1} R\cdot$$

$\underset{\sim}{73}$

Propagation:

$$R\cdot + CCl_4 \xrightarrow{k_2} \underline{RCl} + \cdot CCl_3$$

$$\cdot CCl_3 + \underset{\sim}{73} \xrightarrow{k_3} \underline{CHCl_3} + \underline{\phi_2CO} + N_2 + R\cdot$$

$$R\cdot + \underset{\sim}{73} \xrightarrow{k_4} RH + \phi_2CO + N_2 + R\cdot$$

Termination:

$$2R\cdot \xrightarrow{k_5} \text{Combination}$$

$$2R\cdot \xrightarrow{k_6} \text{Disproportionation}$$

$$R\cdot + \cdot CCl_3 \xrightarrow{k_7} RCCl_3$$

$$2\cdot CCl_3 \xrightarrow{k_8} Cl_3C\text{-}CCl_3$$

To fit the first-order kinetics, we have to assume that the termination step involves the reactions of trichloromethyl radicals with R· radicals. The first-order rate expression is (equation [120]):

$$[120] \quad \text{Rate} = \left(\frac{k_1 k_2 k_3 [CCl_4]}{k_7} \right)^{1/2} \quad [73]$$

In the presence of oxygen, the rate of decomposition of 76 is much higher than that of the corresponding degassed sample of 76. However, we cannot conclude that oxygen actually starts the reactions, because oxygen can react with some intermediate radicals in the reaction to form peroxy radicals which can themselves modify the chain steps and the chain length. But, oxygen is a possible initiator in this case. The largest observed rate factor attributed tentatively to initiation by oxygen in air was about 165 (Table 4) for solutions of 76 in CCl_4.

The chain length of a radical chain reaction depends critically on traces of inhibitors or chain transfer agents. In attempting to see what inhibitors would do in the present chain reactions, a small amount of thiophenol was added to the solution of 76 in carbon tetrachloride. It turned out that a very large rate enhancement was obtained (Table 4). The result is very interesting because thiophenol, a good inhibitor of many radical chain processes, does not inhibit decomposition of 76. In fact, thiophenol (0.02 M) is an effective accelerator of decomposition of 76 in carbon tetrachloride (Table 4). As mentioned previously, there is no isobutane (RH) detected from the decomposition of 76 in carbon tetrachloride. However, isobutane (about 60%) was formed when a small amount of thiophenol (0.02 M) is present. This means that the

Table 4: Kinetics of Decomposition of tert-Butylazodiphenylcarbinol 76 at 35°C

Initial Concentration, M	Reaction Conditions	$k \times 10^4$ sec^{-1}	Correlation Coefficient
0.231	CCl_4, air	25.6 ± 0.40	0.996
0.231	CCl_4, air	18.2 ± 0.20	0.998
0.230	CCl_4, air	34.1 ± 1.20	0.974
0.220	CCl_4, air	36.3 ± 1.90	0.961
0.228	CCl_4, degassed	0.34 ± 0.003	0.997
0.198	CCl_4, degassed	0.45 ± 0.040	0.945
0.253	CCl_4, degassed	0.22 ± 0.004	0.983
0.238	CCl_4, degassed 0.02 M C_6H_5SH	117.0 ± 9.50	0.900
0.243	C_6H_6, degassed	0.093[a] ± 0.0005	0.999
0.243	C_6H_6, degassed	0.093[a] ± 0.0016	0.997
0.457	C_6H_6, degassed	b	—
0.457	C_6H_6, degassed	b	—
0.224	C_6H_6, air	0.201 ± 0.005	0.994

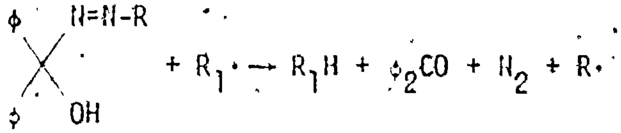
[a] Apparent first-order rate constant. At the initial concentration of tert-butylazodiphenylcarbinol specified only the early points (ca. 0.5 $t_{1/2}$) were slightly off a first-order line through the origin. The plot included points representing up to four half-lives.

[b] Between first- and three-halves order in tert-butylazodiphenylcarbinol but fitting neither.

tert-butyl radical abstracts much more efficiently from thiophenol than from carbon tetrachloride. Phenylthiyl radical is resonance stabilized, thus it is normally unreactive in polymerizing systems except in dimerization. However, in the present case, it acts as a chain carrier by abstracting the hydroxyl hydrogen of 76. This abstracting process must be efficient to account for the high rate. In fact, thiophenol acts as a catalyst in the reaction; tert-butyl radical abstracts hydrogen from thiophenol which is regenerated when the phenylthiyl radical abstracts hydroxyl hydrogen of 76. A chain length of 1000 can be calculated if it is assumed that the rate constant for unimolecular decomposition of 76 in carbon tetrachloride containing thiophenol is the same as the rate constant for decomposition of azoacetate 72 (R = t-butyl) in benzene ($k_1^{35°} = 1.20 \times 10^{-6}\ s^{-1}$) and that the thiophenol did not contain initiators.

Phenol and triphenylstannane were also found not to inhibit the decomposition of 76 both in carbon tetrachloride and in benzene, even though the latter inhibits chain decomposition of compound 1.[20] The enthalpy change of the reaction (equation [121]), calculated without considering the conjugation in benzophenone, is approximately +38 kcal mole^{-1} minus the R_1-H bond energy (see page 92).

[121]



$$\phi_2C(N{=}N{-}R)(OH) + R_1\cdot \rightarrow R_1H + \phi_2CO + N_2 + R\cdot$$

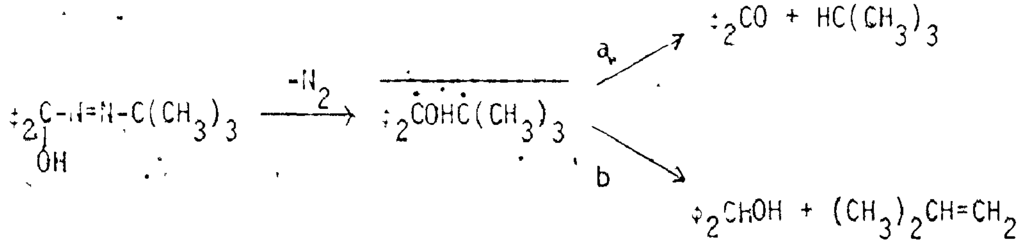
73

When $R_1\cdot$ is phenoxy, phenylthiyl or triphenyl tin radical, ΔH° is calculated to be -37, -34 and -25 kcal mole^{-1}, respectively (see page 93). This indicates that there may not be any stable free radicals that will not attack 73, because they have to form a very weak bond indeed (38 kcal mole^{-1}) in order to have a thermoneutral abstraction step (equation [121]). Such weak bonds, however, are not found in stable molecules. Therefore, in principle, the present reaction is a chain process which is not inhibitable in the normal way; namely, by adding an inhibitor which forms a radical so stable (see page 29 for the mechanisms of inhibitor action) that abstraction by it would be highly endothermic. It might be inhibitable by virtue of a high activation energy required for an exothermic process (equation [121]), $R_1\cdot$ = inhibitor-derived radical), but a search for such inhibitors was not made.

5.2.1.b Decomposition in Benzene

Azocarbinols 73 decompose more slowly at room temperature in benzene than in carbon tetrachloride. The major products are benzophenone and the corresponding compounds RH. It should be noted that the structures of several non-isolable azocarbinols 73 (Table 3) can be established from their decomposition products in benzene (and carbon tetrachloride). For example, 2-hydroxyethyl-α-azodiphenylcarbinol, 73 (R = CH_2CH_2OH) decomposes readily in benzene yielding ethanol and benzophenone as the major products.

The decomposition of 76 in benzene was studied in detail. It was found that the decomposition was not well-behaved. At relatively low concentration of 76 (0.24 M), reproducible first-order kinetics were obtained if air was excluded (Table 4). Higher initial concentrations, however, led to kinetics which fit neither first- nor three-halves order. We can account for this in the following way. There are two competing mechanisms for the decomposition of 76 in benzene. One of them is the unimolecular decomposition (equation [122]). There are two possible paths, a and b, open for the caged radical pair (represented by a solid bar in equation [122]) arising from unimolecular decomposition of 76.

[122] 

$$\phi_2\underset{\displaystyle OH}{C}-N=N-C(CH_3)_3 \xrightarrow{-N_2} \overline{\phi_2\dot{C}OH\,\dot{C}(CH_3)_3} \begin{cases} \xrightarrow{a} \phi_2CO + HC(CH_3)_3 \\ \xrightarrow{b} \phi_2CHOH + (CH_3)_2CH{=}CH_2 \end{cases}$$

Path a involves the formation of benzophenone and isobutane by transfer of a hydrogen atom from the benzhydryl- to the tert-butyl-radical in the cage. Path b yields diphenylcarbinol and isobutene by disproportionation also in the cage. The decomposition of 76 in this way (equation [122]) is, of course, first-order. The other competing mechanism is a chain process (equation [121], R = R_1 = tert-butyl) which involves the attack of tert-butyl radicals at the hydroxyl hydrogen. This induced decomposition should fit three-halves order kinetics. However, it was found that neither mechanism fit the kinetic data, but that both of them were in competition in benzene. The final products agree with the mechanisms reasonably well, accounting for 93% of the tert-butyl groups (91% as isobutane and another 2% as isobutene). The remaining 7% is unaccounted for. Isobutene could be formed by the disproportionation reactions of tert-butyl radicals in the chain termination step and by disproportionation reactions of a radical pair (path b) in equation [122].

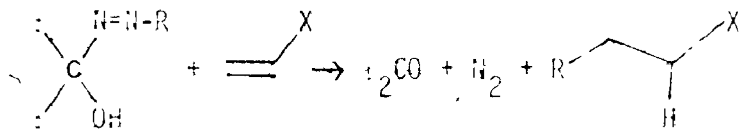
The former source is more likely for two main reasons. First, disproportionation path a (equation [122]) is more likely than path b on thermochemical grounds since path a leads to a C=O bond whereas path b leads to a C=C bond. One piece of evidence in support of path a and against path b is that diphenylhydroxymethyl radicals are not spin trapped by 2-methyl-2-nitrosopropane but are converted instead to benzophenone by transfer of the hydroxyl hydrogen to the nitroso group.[236] Second, the diphenylcarbinol expected from path b could not be detected in the benzophenone fraction by either i.r. or tlc. Since the observed kinetics is between first- and three-halves order in 76, isobutane must arise both from the induced decomposition and from path a (equation [122]), in concentrated solutions of 76.

In the presence of air, the rate of decomposition of 76 in benzene is about twice higher than that of the degassed sample (Table 4). There are several factors accounting for it. First, as discussed in the carbon tetrachloride case, oxygen may be an initiator for the reaction. Second, peroxy radicals, which are certain to be formed from the reactions of oxygen with intermediate radicals, can modify the chain termination steps and, in doing so, the chain length could be increased. The overall apparent rate constant will be affected even for a small amount of such peroxy radicals present. As expected, the p.m.r. spectrum of the product mixture from decomposition of 76 in benzene in the presence of air was complex and included at least four signals slightly downfield from the isobutane doublet. Isobutane was still a major product under conditions of limited oxygen supply (capped nmr tube).

5.2.2 Reactions with Olefins and Azobenzene

The decomposition of 73, in benzene or in carbon tetrachloride solutions, is induced by radicals through abstraction of hydroxyl hydrogen in concert with formation of nitrogen (equation [121]) (see previous section, 5.2.1). This mode of decomposition is analogous to that of compound 1, recently reported from this laboratory by Knittel and Warkentin.[23] The stabilization afforded at the transition state from the combined heats of formation of nitrogen and of benzophenone is sufficient to permit a variety of radicals, even highly stabilized ones, to abstract hydroxyl hydrogen. Consequently, such excellent chain transfer ability of 73 should make them good reagents for radical chain addition yielding small molecules according to equation [123]. The addition of the groups

[123]



73

R and H from 73 according to equation [123] has been successfully demonstrated in a variety of unsaturated compounds, including acrylonitrile, norbornene, crotonaldehyde and azobenzene. The yields are as high as 100 based on 73. The results of reactions of 73 with different olefinic substrates and with azobenzene are gathered in Tables 5, 6, 7, 8 and 9. In many instances, phenol increases the yield of the adducts from decomposition of 73 in the presence of an alkene. The detailed discussion of the role played by phenol in the present radical chain hydroalkylation reactions will be presented in section 5.2.3.

The radical addition mechanism is a complex sequence of steps,

Table 5: Hydro-tert-butylation of Unsaturated compounds

Reactant	Product	Yields %	p.m.r. (in $CDCl_3$)	i.r. (in $CDCl_3$) cm^{-1}	m.s.[g] mol. wt
crylonitrile $CH_2=CHCN$	4,4-dimethylvaleronitrile $(CH_3)_3CCH_2CH_2CN$	63(85)[a] (20)[b]	δ0.93(s,9),δ1.61(t,2,J=7.8Hz) δ2.30(t,2,J=7.8Hz)	2950,2900,2250,1460,1450, 1390,1360,1220,1190,1050	—
methyl vinyl ketone $CH_2=CHCOCH_3$	5,5-dimethylhexan-2-one[c] $(CH_3)_3CCH_2CH_2COCH_3$	31(23)[b]	δ0.89(s,9),δ1.64(t,2,J=9.0Hz) δ2.15(s,3),δ2.48(t,2,J=0.0Hz)	2970,1710,1520,1460,1420, 1365,1290,1245,1205,1060, 1020	128
rotonaldehyde $CH_3CH=CHCHO$	3,4,4-trimethylpentanal $(CH_3)_3CCH(CH_3)CH_2CHO$[d]	32(50)[b]	δ0.89 and δ0.97(s, ^{t}Br(s) and one arm of CH_3(d),12) δ1.54-2.62(m,3), δ9.66(m,1)	2980,2920,2820,2720,1720, 1460,1410,1390,1365,1310, 1280,1220,1180,1125,1170, 1015	128
methyl acrylate $CH_2=CHCO_2CH_3$	methyl-4,4-dimethylvalerate $(CH_3)_3CCH_2CH_2COOCH_3$	8(40)[b]	δ0.88(s,9),δ1.36-1.56(m,2) δ2.10-2.30(m,2),δ3.50(s,3)	2950,2900,1730,1440,1370, 1340,1270,1250,1215,1170, 1145,1060,1020,990	—
isopropenylacetate $CH_2=C(CH_3)O_2CCH_3$	2-acetoxy-4,4-dimethylpentane $(CH_3)_3CCH_2CHCH_3O_2CCH_3$	18(12)[b]	δ0.91(s,9),δ1.20(d,3,J=6.1Hz) δ1.40-1.78(m,3),δ2.01(s,3)	2980,1720,1470,1365,1270, 1210,1125,1060,1025	158
norbornene	exo-2-tert-butylbicyclo[2,2,1]heptane	25(0)[b]	δ0.87(s,9),δ0.96-1.60(m,9) δ2.05-2.30(m,2)[e]	2950,2850,1460,1390,1370 1305,1280,1100,1020,860, 825	152
trans-stilbene $C_6H_5CH=CHC_6H_5$	2,2-dimethyl-3,4-diphenylbutane[f] $C_6H_5CH_2CH(C_6H_5)C(CH_3)_3$	0	—	—	—

a The bracketed number is the yield of crude product from a run with phenol present, mol ratio phenol:76 = 0.5

b The number in parentheses is the yield of crude product from a run with phenol present, mol. ratio phenol:76 = 1.0

c 2,4-Dinitrophenylhydrazone melted at 105-106°C (lit.[237] m.p. 105-106°C).

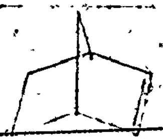
d 2,4-Dinitrophenylhydrazone melted at 110°C (lit.[238] m.p. 112-112.5°C).

e The pmr spectrum (CCl_4) reported in the literature[239] is in good agreement with our spectrum.

f Expected but not formed.

g The mass spectra all showed m/e 57 due to $(CH_3)_3C^+$.

Table 6: Hydro-isopropylation of Unsaturated Compounds

Reactant	Product	Yields %	p.m.r. (in $CDCl_3$)	i.r. (in $CDCl_3$) cm^{-1}	m.s.[g] mol. wt
acrylonitrile $CH_2=CHCN$	4-methylvaleronitrile $(CH_3)_2CHCH_2CH_2CN$	53(75)[a]	δ0.91(d,6,J=6.5Hz) δ1.42-1.72(m,3) δ2.31(t,2,J=7Hz)	2950,2900,2245,1425,1360, 1320,1280,1245,1170,1120, 1025	97
methyl vinyl ketone $CH_2=CHCOCH_3$	5-methylhexan-2-one[b,c] $(CH_3)_2CHCH_2CH_2COCH_3$	13(11)[a]	δ0.85(d,6,J=6.0Hz) δ1.37-1.58(m,3) δ2.08(s,3), δ2.38(t,2,J=7Hz)	2950,2900,1710,1410,1350, 1270,1230,1170,1125,1005	114
crotonaldehyde $CH_3CH=CHCHO$	3,4-dimethylpentanal[d] $(CH_3)_2CHC(CH_3)HCH_2CHO$	35(43)[a]	δ0.81(d,6,J=6.5Hz) δ1.01(d,3,J=4.0Hz) δ1.40-2.52(m,4) δ0.69(t,1,J=3.0Hz)	2900,2820,2720,1720,1410, 1370,1290,1240,1210,1150, 1110,1040	114
methyl acrylate $CH_2=CHCO_2CH_3$	methyl-4-methylvalerate $(CH_3)_2CHCH_2CH_2CO_2CH_3$	5(32)[a]	δ0.77(d,6,J=6.0Hz) δ1.34-1.47(m,3) δ2.18(d,2,J=7.0Hz) δ3.55(s,3)	2900,2850,1720,1430,1350, 1325,1290,1265,1220,1190, 1175,1105	130
isopropenyl acetate $CH_2=C(CH_3)O_2CCH_3$	2-acetoxy-4-methylpentane $(CH_3)_2CHCH_2C(CH_3)HO_2CCH_3$	15(10)[a]	δ0.85(d,6,J=6.5Hz) δ1.15(d,3,J=6.5Hz) δ1.24-1.66(m,3) δ1.96(s,3), δ4.78-5.06(m,1)	2900,1710,1420,1350,1270, 1230,1065,1125,1060,1040, 1025	144
norbornene 	exo-2-isopropyl-bicyclo- [2,2,1]heptane	22(0)[a]	δ0.74(d,6,J=7Hz) δ0.78-1.46(m,11) δ2.10(broad s,2)	2900,1445,1360,1320,1280, 1240,1170,1160,1140,1035, 1025,1000	138

[a] The number in parentheses is the yield of crude product from a run with phenol present, mol. ratio phenol:**73** (R=isopropyl)=1.0.

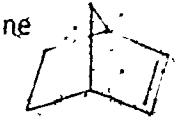
[b] The p.m.r. and i.r. spectra were in good agreement with those reported in the literature.[240]

[c] 2,4-Dinitrophenylhydrazone melted at 90-91°C (lit.[241] m.p. 92-93°C).

[d] 2,4-Dinitrophenylhydrazone melted at 92°C (lit.[242] m.p. 93-94°C).

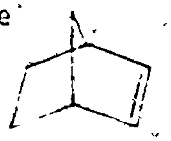
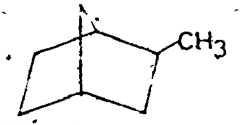
[e] The mass spectra all showed m/e 43 due to $(CH_3)_2CH$.

Table 7: Hydroethylation of Unsaturated Compounds

Reactant	Product	Yields	p.m.r.	i.r. cm^{-1}	m.s. mol. wt.
acrylonitrile $CH_2=CHCN$	valeronitrile[b] $CH_3CH_2CH_2CH_2CN$	37(55)[a]	δ0.83-1.13(m,3) δ1.37-1.90(m,4) δ2.20-2.43(m,2)	2950,2900,2250,1465,1430, 1380,1245,1325,1300,1110, 1035,935,918,675	———
crotonaldehyde	3-methylpentanal[c,d]	34(42)[a]	δ0.90(t,3,J=7Hz) δ0.96(d,3,J=7Hz) δ1.18-1.50(m,3),δ1.83-2.16 (m,1),δ2.16-2.54(m,2) δ9.74(t,1,J=2Hz)	2950,2890,2820,2720,1720, 1460,1420,1380,1290,1250, 1210,1135,1025,970,885, 855 ($CDCl_3$)	———
methyl acrylate $CH_2=CHCO_2CH_3$	methylvalerate[e] $CH_3CH_2CH_2CH_2CO_2CH_3$	5(13)[a]	δ0.82-0.99(m,3) δ1.17-1.77(m,4) δ2.24-2.35(m,2) δ3.60(s,3)	2950,2860,1725,1440,1360, 1320,1265,1200,1175,1135, 1110,1020 ($CDCl_3$)	116
isopropenylacetate $CH_2=C(CH_3)O_2CCH_3$	2-acetoxypentane $CH_3CH_2CH_2CH(CH_3)O_2CCH_3$	9(7)[a]	δ0.84-0.98(m,3) δ1.20(d,3,J=7Hz) δ1.30-1.63(m,4) δ2.00(s,3) δ4.82-5.01(m,1)	2950,2850,1725,1450,1370, 1250,1125,1060,1025,955, 885 ($CDCl_3$)	130
norbornene 	exo-2-ethyl-bicyclo-[2,2,1]heptane	35(6)[a]	δ0.74-1.51(m,14) δ1.95(m,1) δ2.16(m,1)	2950,2900,1450,1420,1370, 1325,1300,1285,1225,1135, 922,860,693	124

[a] The number in parentheses is the yield of crude product from a run with phenol, mol. ratio phenol:73 (R=ethyl) = 1.0
[b] The p.m.r. and i.r. spectra were in good agreement with those reported in the literature.[243]
[c] 2,4-Dinitrophenylhydrazone melted at 93-94°C (lit.[244] m.p. 93.5-94.5°C).
[d] The i.r. spectrum was in good agreement with those reported in the literature.[245]
[e] The p.m.r. and i.r. spectra were in good agreement with those reported in the literature.[246]

Table 8: Hydromethylation of Unsaturated Compounds

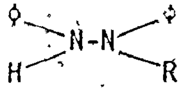
Reactant	Product	Yields	p.m.r. ($CDCl_3$)	i.r. cm^{-1}
acrylonitrile $CH_2=CHCN$	n-butyronitrile[b] $CH_3CH_2CH_2CN$	32(52)[a]	δ1.09(t,3,J=7Hz) δ1.45-1.90(m,2) δ2.38(t,2,J=7Hz)	3000,2920,2250,1470, 1430,1390,1290,1250, 1095 ($CDCl_3$)
isopropenylacetate $CH_2=C(CH_3)O_2CCH_3$	2-acetoxybutane[c] $CH_3CH_2CH(CH_3)O_2CCH_3$	13	δ0.90(t,3,J=7Hz) δ1.22(d,3,J=7Hz) δ1.37-1.70(m,2), δ2.03(s,3) δ4.67-5.00(m,1)	2950,2920,1720,1450, 1370,1250,1130,1030, 1030,880 ($CDCl_3$)
norbornene 	exo-2-methyl- bicyclo[2,2,1]heptane[d] 	59	δ0.80-1.53(m,12) δ1.83(m,1) δ2.16(m,1)	2950,2875,1480,1460, 1455,1375,1350,1368, 1358,1145,1070,925, 910,665

[a] The number in parentheses is the yield of crude product from a run with phenol present, mol. ratio phenol:73(R=CH = 1.0

[b] The p.m.r. and i.r. spectra were in good agreement with those reported in the literature.[247]

[c] The p.m.r. and i.r. spectra were in good agreement with those reported in the literature.[248]

[d] The δ values of ^{13}Cmr were 43.04(C-1), 36.41(C-2), 39.89(C-3), 36.99(C-4), 30.07(C-5), 28.77(C-6), 34.82(C-7), 22.37(CH_3 group). The ^{13}Cmr spectrum was in good agreement with that reported in the literature.[249]

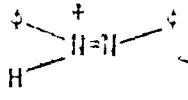
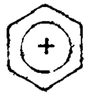
Table 9: Yields and Properties of Substituted 1,2-Diphenylhydrazines 

R	Yield %	M.P. °C	p.m.r.	i.r. cm^{-1}	m.s. mol. wt.^{a}	Analysis
tert-butyl^{b}	100(40 isolated)	52-53 (lit.^{250} 57-57.6)	δ1.10(s,9) δ5.47(s,1) δ6.50-7.20(m,10)	3330,3040,3000,1600, 1495,1450,1400,1365, 1308,1265,1200,1080, 1025,880,650	240	$C_{16}H_{20}N_2$ Calcd. Found N:11.67 11.62
isopropyl	100(45 isolated)	86-87 (lit.^{250} 88.0-88.4)	δ1.07(d,6,J=7Hz) δ4.09(qe,1,J=7Hz) δ4.98(s,1) δ6.47-7.04(m,10)	3310,3050,2970,1925, 1830,1760,1680,1600, 1490,1450,1430,1380, 1360,1320,1300,1270, 1190,1165,1155,1125, 1085,1065,1035,1025, 860,688	226	—
ethyl	100(23 isolated)	40-41 (lit.^{251} 38-40)	δ1.23(t,3,J=7Hz) δ3.56(q,2,J=7Hz) δ5.40(s,1) δ5.57-7.25(m,10)	3320,3040,2960,1925, 1825,1760,1700,1600, 1490,1450,1370,1340, 1300,1250,1185,1170, 1155,1130,1075,1035, 1025,860,690	212	—
methyl	60(27 isolated)	73.5-74.5 (lit.^{250} 74.0-74.5)	δ3.10(s,3) δ5.23(s,1) δ6.53-7.25(m,10)	3320,3040,2950,2850, 2800.1925,1825,1760, 1600,1490,1450,1300, 1250,1185,1170,1155, 1115,1080,1030,880, 690	198	—
phenyl	40	138.5-139.5 (lit.^{252} 141-142)	δ5.93(s,1) δ6.63-7.27(m,15)	3320,3030,1925,1840, 1770,1580,1540,1490, 1455,1430,1310,1275, 1230,1175,1155,1075, 1030,910,880,690	260	—

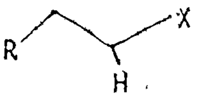
Continued......

Table 9 (Continued)

R	Yield %	M.P. °C	p.m.r.	i.r. cm^{-1}	m.s. mol. wt.[a]	Analysis
cyclohexyl	48	108-109	δ1.00-2.00(m,10) δ3.76(m,1) δ5.30(s,1) δ6.60-7.27(m,10) (in $CDCl_3$)	3320,3050,2950,2900, 1925,1830,1770,1700, 1600,1490,1450,1430, 1380,1335,1310,1280, 1230,1175,1150,1080, 1035,1025,897,892, 880,696,663	266	$C_{18}H_{22}N_2$ Calcd. Found C:81.15 80.73 H: 8.33 8.73 N:10.52 11.08
2-hydroxyethyl	33(based on azo-acetate used)	71-72	δ1.86(s,1) δ3.71(t,2,J=6Hz) δ3.97(t,2,J=6Hz) δ5.90(s,1) δ6.72-7.40(m,10) The spectrum was taken in $CDCl_3$. Peaks at δ1.86 and δ5.90 disappeared when shaking with D_2O.	3620,3320,3030,2930, 3850,1925,1825,1760, 1600,1490,1455,1330, 1300,1235,1210,1195, 1180,1160,1080,1060, 1030,910,880,690	228	$C_{14}H_{16}N_2O$ Calcd. Found C:73.64 73.49 H: 7.07 7.17 N:12.28 12.27

[a] The mass spectra all showed the molecular ion and have m/e 183 due to  as well as m/e 77 due to 

[b] The elemental analysis was done by A.B. Gygli Microanalysis, Ltd., Toronto.

as shown in Scheme I (page 19). The desired product R  (equation [123]) is formed by the chain propagation steps. The chain length must therefore be as long as possible so that termination products form a small part of the total products. Both the addition and abstraction, in propagation steps, must be very fast since the terminations are very fast in solution (see section 1.4.2). Therefore, both propagation steps must be exothermic or, at worst, only slightly endothermic for them to be very efficient.

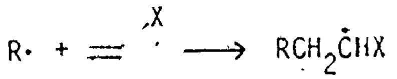
Consider two propagation steps, as depicted in Scheme IX (page 92) of the decomposition of 73 in the presence of an olefin or azobenzene. The enthalpy change of step 1 (addition) comes to be about -20 kcal mole^{-1} in case of olefins, or -12 kcal mole^{-1} for azobenzene. The calculation did not consider any effects stabilizing the new radical resulting from the addition, e.g., the adduct radical formed by R· adding to azobenzene is stabilized by hydrazyl resonance as well as benzyl resonance. The values of bond energies for the calculation were taken from the text by Cram[253] (unless otherwise indicated). The enthalpy of step 2 (abstraction) calculated without considering conjugation in benzophenone is approximately -32 to -61 kcal mole^{-1}. The calculation of the enthalpy change for both steps is shown in Scheme IX (page 93), together with the reactions. Both steps calculated are exothermic hence addition to unsaturated compounds could be very efficient.

Azobenzene was found to be a good substrate to trap various alkyl radicals (i.e., carbon-centered radicals) generated from 73 (Table 9). Radical addition across the N=N bridge in azo compounds yielding substituted hydrazines is currently rare (as reviewed on page 25). The

Scheme IX

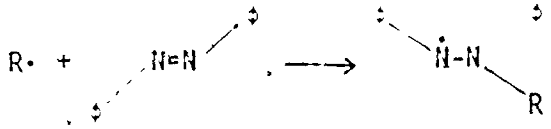
(All values are in Kcal mole^{-1})

Step 1


R·
$RCH_2\dot{C}HX$
X

ΔH°_1 = energy loss (C=C) - energy gain (2 x C-C)

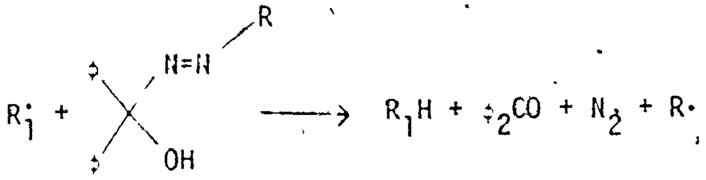
= 146 - 2 x 83 = -20



ΔH°_2 = energy loss (N=N) - energy gain (C-N + N-N)

= 100 - (73 + 39) = -12

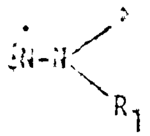
Step 2


$R_1^\cdot$
R
N=N
OH
R_1H + $_2CO$ + N_2 + R·

Energy Loss		Energy Gain	
O-H	111	R_1-H	
C-O	86	C=O	179
2 x C-N	146	N N	226
N=N	100		
Total:	443	Total:	$D(R_1\text{-}H)$ + 405

$\therefore$ ΔH°_3 = 38 - $D(R_1\text{-}H)$

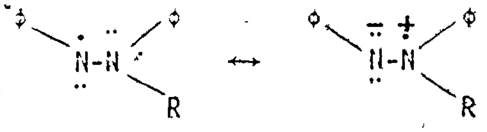
Continued......

$R_1^{\bullet}$	R_1-H	ΔH_3°
$R_1CH_2\dot{C}HX$	99	-61
	70[a]	-32
:S•	75[illegible]	-37
:O•	72[b]	-34
ϕ_3Sn•	63[illegible]	-25

[a] The value for the strength of the N-H bond in DPPH-H (diphenyl-picryl-hydrazine) was used.[256]

[b] The value for the strength of the O-H bond in 2,4,6-tri-t-butylphenol was employed.[256]

present results are therefore significant. The yields with azobenzene in many cases are quantitative based on 73 (Table 9). Two main reasons account for the facile addition to azobenzene. Firstly, steric hindrance in the adduct radical is not severe because the bond angles at both nitrogens are expected to be approximately 120° on the basis of known angles in diphenylpicrylhydrazyl.[254] Second, the hydrazyl radical is stabilized by hydrazyl resonance as well as benzyl resonance (equation [124]). The transition state for addition would have to be

[124] 

product-like to gain most of the available hydrazyl resonance, as a rotation about the N-N bond is required to bring the originally orthogonal lone pair and the π-orbital into conjugation. We have not found estimates or experimental values in the literature for the magnitude of hydrazyl stabilization. That it is large is suggested by the spin density distribution estimated from the esr splittings of hydrazyl radicals. Ingold[257] has stated that, in all authentic hydrazyls, "the splitting constants of the two nitrogens are of comparable magnitude and are generally in the range of 6-12 gauss". Attempts to observe the adduct hydrazyl radical with e.s.r. spectroscopy in the course of reactions of azobenzene with 76 in carefully degassed benzene or chlorobenzene solution at low temperatures were not successful. The failure might be due to the fact that the second step, abstraction of the hydroxyl hydrogen from 76, is too fast, which thus destroys the hydrazyl radical very efficiently.

Decomposition of 76 in the presence of trans-stilbene, a close analog of azobenzene, did not lead to the desired product, 1,2-diphenyl-3,3-dimethylbutane (Table 5). The contrast between these two cases could come from a large dependence of either propagation rate constant on the structure of the unsaturated acceptor molecule. That it is the addition step which is responsible was indicated clearly by the finding that isobutane, which is not formed in reaction of 76 with azobenzene, is a major product of decomposition of 76 in the presence of stilbene. Apparently, tert-butyl radicals prefer abstraction of hydrogen from 76 over addition to stilbene, even though the latter is present in higher concentration. This could be the result of a low rate constant for addition to stilbene or of reversibility of the addition step. Slow addition or ready reversibility, whichever is applicable, must result partly from steric hindrance in the adduct radical, 1,2-diphenyl-3,3-dimethylbutyl radical. On the contrary, the adduct radical, 1,2-diphenyl-tert-butylhydrazyl, is readily stabilized both by hydrazyl and benzyl resonances. If such stabilization by hydrazyl resonance is substantial, then even a fraction of it available at the transition state could be sufficient to account for the very different behaviours of azobenzene and stilbene toward tert-butyl radicals.

It is observed (in Tables 5, 6, 7 and 8) that the yield of the hydroalkylation of norbornene increased in the following order:

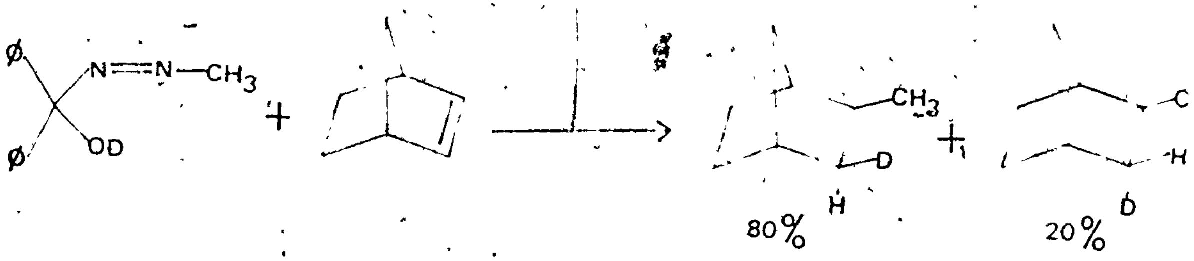
$$\dot{C}H_3 < CH_3\dot{C}H_2 < (CH_3)_2\dot{C}H < (CH_3)_3\dot{C}$$

This order might reflect the steric hindrance in the addition as well as the stability of the adduct radicals formed. Methyl radical is considerably less bulky than tert-butyl radical, so the attack (exo) on the norbornene skeleton is relatively easy. Besides, the intermediate adduct radicals are secondary and, by virtue of favourable thermochemistry, efficient addition of primary radicals such as methyl and ethyl radicals would be expected. For secondary and tertiary radicals (like isopropyl and tert-butyl radicals), on the other hand, the addition step would be either thermoneutral or endothermic. Consequently, the addition will not be efficient. The alkyl groups in the resulting 2-alkylnorbornanes are in the exo position as deduced from ^{13}Cmr spectroscopy (Table 8).

The regiochemistry of addition to unsymmetric olefins is that expected for a mechanism which involves addition of a radical so as to form the most stable radical adduct (i.e., Kharasch[7] addition), which subsequently abstract hydrogen from 73. The direction of addition is almost invariably the opposite to that encountered in ionic Markovnikoff addition, so that synthesis by the radical route is complementary to ionic addition.

Synthesis of monodeutero compounds using hydroxyl deuteriated 73 is another obvious potential utility of 73. This has been demonstrated in the following example. Shaking 73 (R = CH_3) in benzene with D_2O exchanges the hydroxyl hydrogen for deuterium. Trapping reactions were subsequently carried out, in the two-phased system, with norbornene. More than 87 atom % deuterium (estimated by mass spectrometry[258]) was incorporated into the resulting product which was obtained in 50% yield (equation [125]). There are two peaks, separated by 0.5 ppm, in the ^{2}Hmr

[125]

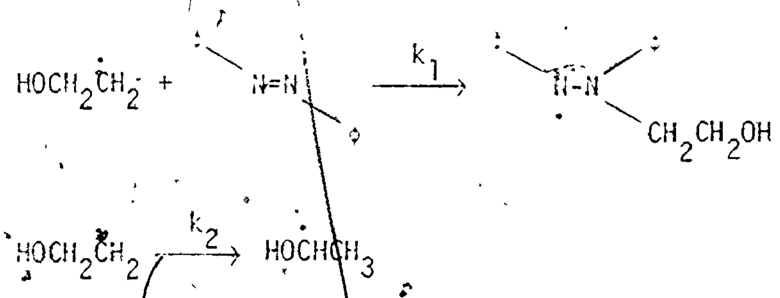


spectrum of the product.[259] Electronic integration gives a ratio of 1:4 for these peaks. The exo:exo assignment to major product (equation [125]) is based on the analogy for the exo-exo addition of ethyl bromoacetate to norbornene[118] (page 23). Therefore, relatively easy and cheap monodeuteriation of compounds can be accomplished with **73**.

The generation of 2-hydroxyethyl radical from **73** (R = CH_2CH_2OH) is important. Hydrogen abstraction from alcohols in solution always occurs from the carbon atom bearing the hydroxyl group (see page 24). The resulting 1-hydroxyalkyl radicals are indeed observed by e.s.r. spectroscopy.[32] 2-Hydroxyethyl radical was mentioned by Gray and Herod[96] who measured the rates of hydrogen abstraction, in the gas phase, by methyl radical from the three different sites in ethanol. At 150°C, 75% of the hydrogen comes from the methylene group, 20% from OH, and about 5% from the methyl group.

The 2-hydroxyethyl radical from **73** (R = CH_2CH_2OH) can be trapped with nitrosobenzene as spin trap (see section 5.2.4). Also, the total fragments CH_2CH_2OH and H are captured with azobenzene to form 1,2-diphenyl-1-β-hydroxyethylhydrazine (Table 9). It is well known that primary and secondary alcohols add to unsaturated compounds to form secondary and tertiary alcohols, respectively (see page 24). The present addition of ethanol to azobenzene via 2-hydroxyethyl radical is the only example of addition of a primary alcohol (except methanol) to give a primary alcohol product. Rearrangement of 2-hydroxyethyl to 1-hydroxyethyl radicals is very unlikely in the present situation. With a large excess of azobenzene and a large rate constant for addition because of the formation of a resonance stabilized hydrazyl radical, the rate of capture of 2-hydroxyethyl radical by azobenzene should be much faster than the rearrangement process, i.e., $k_1 >> k_2$ (equation [126]).

[126]



Moreover, as reviewed in section 1.4.1 b, the 1,2-hydrogen shift in free radical chemistry very seldom occurs.

It has been reviewed (page 24) that very few hydrocarbons are known to add to unsaturated compounds effectively. In the present thesis, the addition of hydrocarbons as well as ethanol to unsaturated compounds has been successfully demonstrated using azocarbinols 73 as the reagents. A general principle regarding radical pathways in synthesis can thus be formulated from the present results (Tables 5-9). "If the radical chain addition of a reagent X-Y to unsaturated systems is impractical because of the adverse thermochemistry of the chain carrying abstraction step, it can be made more favourable and practical by using a new reagent, X-A-B-Y, which delivers fragments X and Y in a chain reaction by virtue of altered thermochemistry from formation of stable co-product(s) A=B in the propagation step in which Y is added." In the case of azocarbinols

73, the fragments X and Y are R and H, respectively, which are delivered by virtue of the combined heats of formation of nitrogen and of a carbonyl group (i.e., CO in benzophenone). Another advantage of using 73 is that the two fragments R and H are added in two discrete operations. This eliminates any complications due to cage reactions, such as radical combination (or disproportionation) of R and H to give RH.

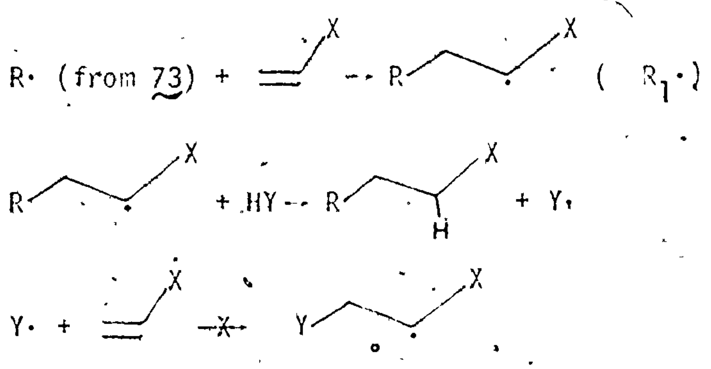
Potential fragments, X and Y, are numerous. In principle, XY can be any organic or inorganic compound. Stable coproduct(s) with high heats of formation include molecular nitrogen, CO_2, CO, R_2CO, SO_2 and aromatic molecules.

In theory, the synthetic potential of 73 is vast. However, it has been observed that several azocarbinols 73 (R = cyclohexyl, phenyl, 2-hydroxyethyl, allyl, benzyl) did not form adducts, in the sense of equation [123], with norbornene, acrylonitrile and crotonaldehyde. Moreover, compounds 73 (R = allyl or benzyl) did not form desired substituted hydrazines with azobenzene. A major known cause of failure is polymerization. In the cases of allyl and benzyl radicals (which are resonance stabilized), another reason for failure is perhaps their reluctant addition to unsaturated compounds. Whether or not the expected adducts were actually formed in some cases but were not stable enough to be isolated, is unknown. In any case, the scope of 73 as practical synthetic reagents is limited.

5.2.3 Reactions with Olefins in the Presence of Phenol

A significant complication in radical additions to olefins according to Scheme I (page 19) is polymerization. One way to overcome this problem, studied extensively by Minisci,[104] is to carry out the reactions in the presence of a redox system such as Fe^{3+} or Cu^{2+}. In the present thesis, we tackled this problem by choosing selective chain transfer agents (HY), which function as good hydrogen donors like azocarbinols 73, to decrease the lifetime of adduct radicals, thereby suppressing polymerization. Such agents would have to react more slowly with R· than with R_1· and the radical Y· would have to be capable of abstracting hydrogen from 73 but not of addition to $=\!\!\diagup^{X}$ (equation [127]). A reagent meeting those requirements would really be a catalyst in the radical chain additions to olefins.

[127]



$$Y\cdot + 73 \rightarrow HY + \phi_2CO + N_2 + R\cdot$$

Phenol was found to be one of the reagents (HY) mentioned above. In many cases, phenol increases the yield of the addition product (Tables 5-8) from decomposition of 73 in the presence of an olefin. The yields of the adducts were reduced with added phenol in some cases because of competitive reactions existing for R· radicals (from 73); the radicals R· can be intercepted by phenol before addition to olefins occurred (equation [128]). The concentration of phenol required for optimizing

[128] $\cdot R\cdot\ (\text{from } 73) + :OH \rightarrow \cdot O\cdot + RH$

the yield of adduct is expected to be different for each unsaturated substrate because the rate constants for abstraction from phenol, for polymerization, and for chain termination are structure dependent. The optimization experiments will be discussed later in this section.

Reported catalysis in radical chain addition is currently rare (as reviewed in section, 1.9), and the present discovery is therefore important. The reason for the rarity of such catalysis is obvious by considering the features which allow phenol to play a catalytic role in the present case. Phenol is a good hydrogen donor to radicals largely because the resulting phenoxy radicals are resonance stabilized. Thus, phenoxy radicals are very poor at radical substitution and will not normally accomplish the chain transfer step required to complete a catalytic role. Their sluggishness in radical addition and radical substitution steps is of course, the basis of the normal inhibitory function of phenols in radical processes. However, induced decomposition of 73 is exceedingly exothermic by virtue of the combined heats of formation of nitrogen and benzophenone. Such a favourable enthalpy change, partly available at the transition state, is sufficient to permit the efficient abstraction by phenoxy radicals. Therefore, phenol acts as a catalyst for the present hydroalkylation process.

More important, probably, is a general principle that can be stated based on the present results. "Compounds (Y-B) may act as catalysts for the radical chain addition of A-B to unsaturated substrates only if both chain transfer steps, $Y\text{-}B + R\cdot \rightarrow Y\cdot + BR$ and $A\text{-}B + Y\cdot \rightarrow A\cdot + Y\text{-}B$, are very efficient."

Optimization experiments have been performed, using the reactions of 73 (R = isopropyl) with crotonaldehyde and with acrylonitrile as examples. The results of plotting the yield of adducts against the concentration of phenol are shown in Figures I and II. All the curves thus plotted have a similar shape. The curves exhibit a maximum, within the experimental limits of phenol concentration, which occurs at approximately 1.3-1.5 M phenol concentration. The highest curves occur in both cases whenever the concentration of olefin was about 2 M. The initial concentration of 73 (R = isopropyl) was kept constant (0.348 M) throughout both experiments but other work (Fig. III) showed that the yield of adduct is insensitive to the concentration of azocarbinol in the concentration range that was employed. Thus, based on the above observation, we suggest that a near optimum condition to obtain high yields of adducts is when the concentration ratio of 73 (R = isopropyl):phenol:olefin equals 1:4:6 and when the absolute concentration of olefin is about 2 M.

The kinetic sequence of reactions is shown in Scheme X. Unfortunately, we have encountered difficulties in attempting to explore this catalyzed chain reaction on a quantitative basis. At the present time, only the empirical results are reported in the previous paragraph.

Plotting the yield of adduct against the ratio [Olefin]/[73] (R = isopropyl) in the absence of phenol gave two curves, which are completely different in shape (Figure IV). In the case of acrylonitrile, the yield decreases as the ratio [olefin]/[73] (R = isopropyl) increases. This reduction of yield is largely because the ratio of the rate of the transfer step to that of polymerization becomes smaller as [olefin]

Figure I Plots of Yield of the Adduct vs. Concentration of Phenol in the Reactions of $:_2\underset{\text{OH}}{\text{C}}\text{H=N-CH(CH}_3)_2$ (0.348 M) with Crotonaldehyde

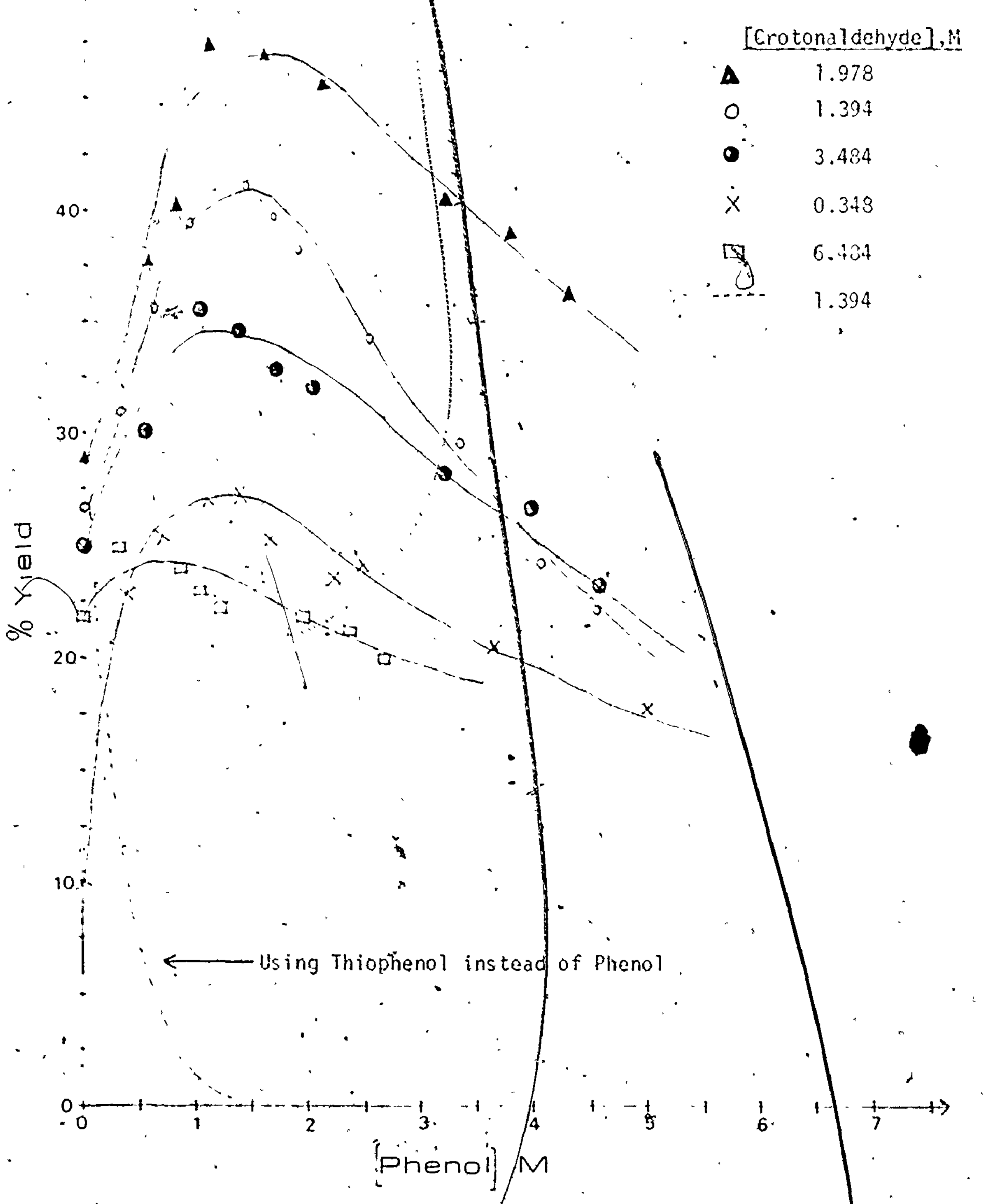


Figure II Plots of Yield of the Adduct vs. Concentration of Phenol in the Reactions of $\phi_2\underset{\substack{|\\ \mathrm{OH}}}{\mathrm{C}}\mathrm{H{=}N{-}CH(CH_3)_2}$ (0.348 M) with Acrylonitrile

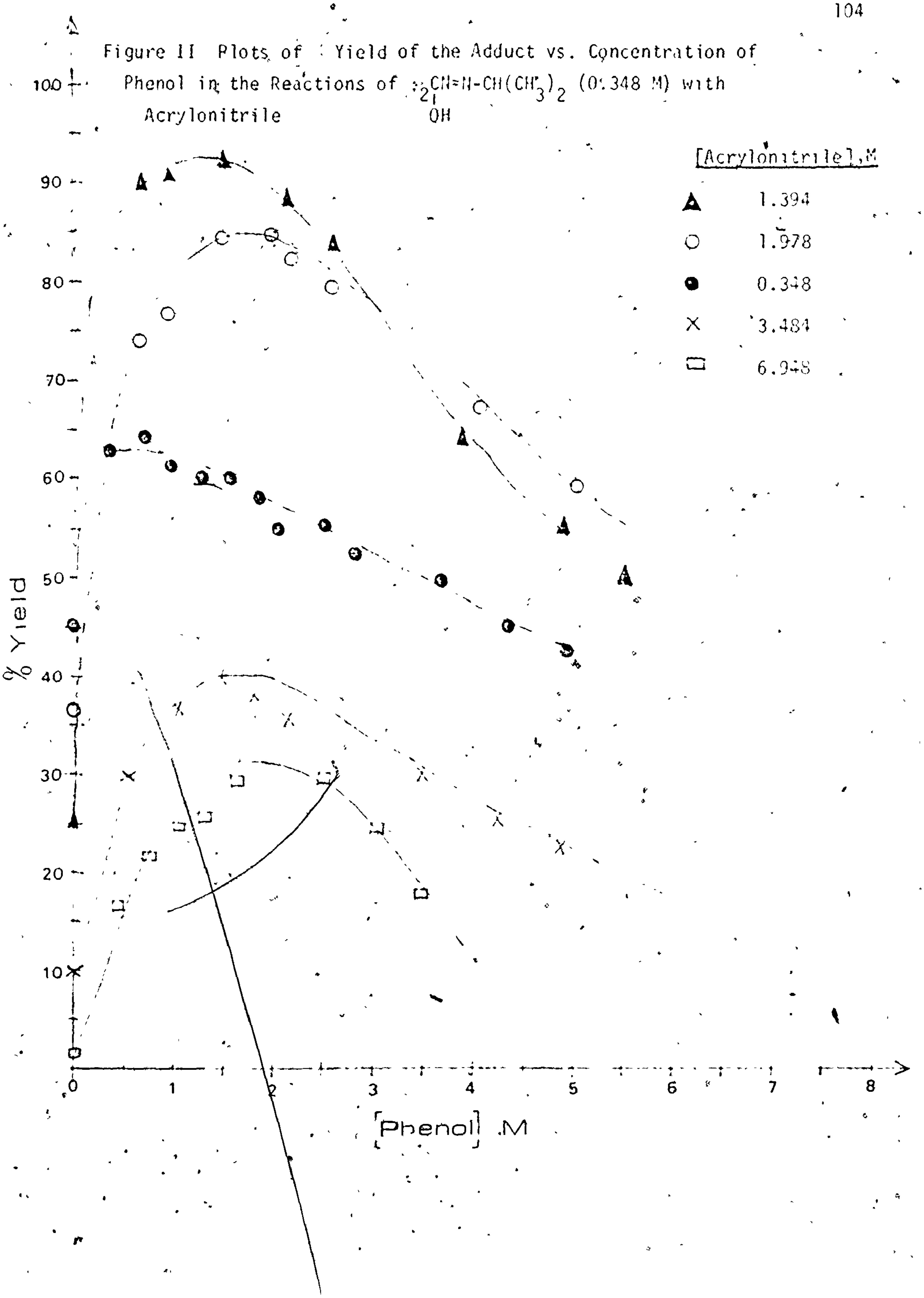


Figure III Plots of Yield of the Adducts vs. Initial Concentration of $\phi_2\underset{\overset{|}{OH}}{C}H=N-CH(CH_3)_2$

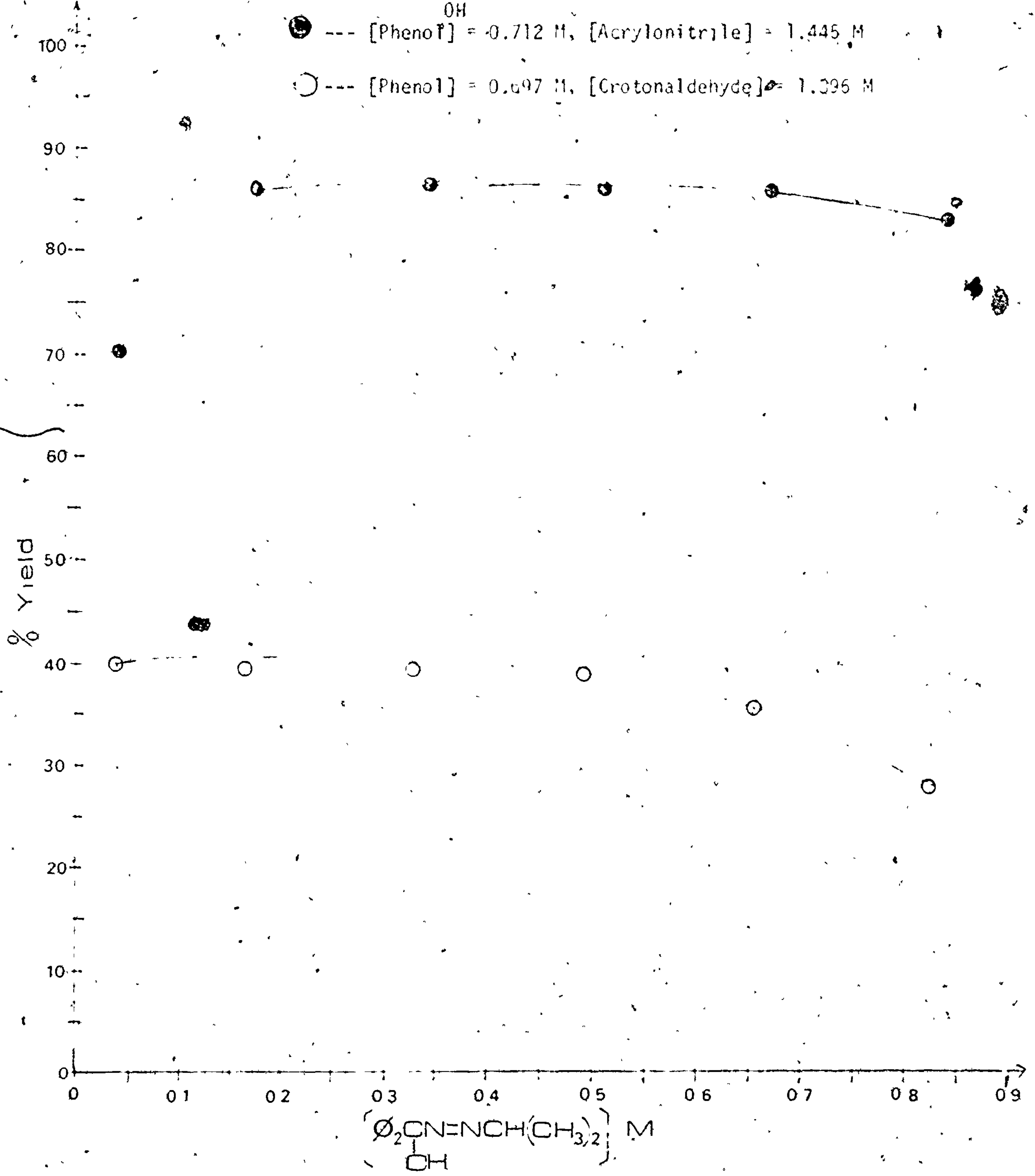
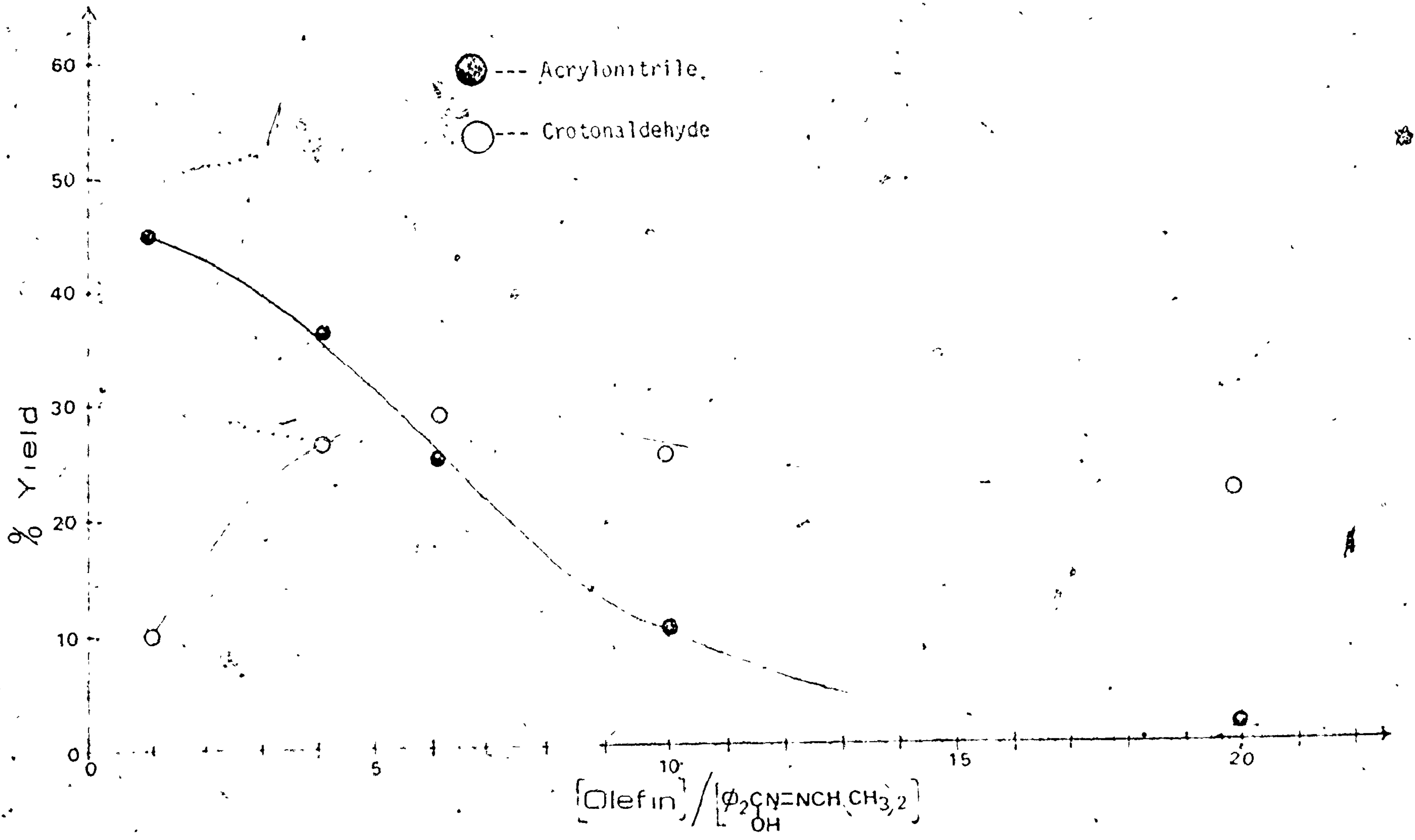


Figure IV Plots of Yield of the Adducts vs. $[\text{Olefin}]/[\phi_2\underset{OH}{C}N{=}N\text{-}CH(CH_3)_2]$

$[\phi_2\underset{OH}{C}N\text{-}N\text{-}CH(CH_3)_2] = 0.348$ M



Scheme X

Initiation: $\mathbf{73}\ (R{=}\text{isopropyl}) \xrightarrow{k_1} R\cdot + \phi_2CO + N_2$

$\mathbf{I}$

Propagation:

$\mathbf{I} + \phi O\cdot \xrightarrow{k_2} \phi OH + \phi_2CO + N_2 + R\cdot$

$R\cdot + \text{Olefin} \xrightarrow{k_3} A\cdot \quad (A \equiv \text{Adduct})$

$A\cdot + \mathbf{I} \xrightarrow{k_4} R\cdot + \phi_2CO + N_2 + \text{Adduct}$

$A\cdot + \phi OH \xrightarrow{k_5} \phi O\cdot + \text{Adduct}$

$R\cdot + \phi OH \xrightarrow{k_6} \phi O\cdot + RH$

$R\cdot + \mathbf{I} \xrightarrow{k_7} RH + \phi_2CO + N_2 + R\cdot$

$A\cdot + \text{Olefin} \xrightarrow{k_8} D\cdot \quad (D \equiv \text{Dimer})$

$D\cdot + \mathbf{I} \xrightarrow{k_9} \text{Dimer} + \phi_2CO + N_2 + R\cdot$

$D\cdot + \phi OH \xrightarrow{k_{10}} \text{Dimer} + \phi O\cdot$

$D\cdot + \text{Olefin} \xrightarrow{k_{11}} T\cdot \quad (T \equiv \text{Trimer})$

$T\cdot + \mathbf{I} \xrightarrow{k_{12}} \text{Trimer} + \phi_2CO + N_2 + R\cdot$

$T\cdot + \phi OH \xrightarrow{k_{13}} \text{Trimer} + \phi O\cdot$

$T\cdot + \text{Olefin} \xrightarrow{k_{14}} M_4^{\cdot} \quad (M_4 \equiv \text{polymer from 4 molecules of olefin})$

$M_p^{\cdot} + \text{Olefin} \xrightarrow{k_p} M_{p+1}^{\cdot}$

$M_p^{\cdot} + \phi OH \xrightarrow{k_{p+1}} M_p + \phi O\cdot$

$M_p^{\cdot} + \qquad \xrightarrow{k_{p+2}} M_p + \phi_2CO + N_2 + R\cdot$

Termination:

$A\cdot + \phi O\cdot \xrightarrow{k_{15}} AO\phi$

$A\cdot + A\cdot \xrightarrow{k_{16}} AA$

Continued......

Scheme X (Continued)

$$\mathrm{A\cdot} + \mathrm{R\cdot} \xrightarrow{k_{17}} \mathrm{AR}$$

$$\phi\mathrm{O\cdot} + \mathrm{R\cdot} \xrightarrow{k_{18}} \mathrm{RO}\phi$$

$$\phi\mathrm{O\cdot} + \phi\mathrm{O\cdot} \xrightarrow{k_{19}} \phi\mathrm{OO}\phi$$

$$\mathrm{R\cdot} + \mathrm{R\cdot} \xrightarrow{k_{20}} \mathrm{RR}$$

$$\mathrm{M}_p^\cdot + \mathrm{M}_q^\cdot \xrightarrow{k_{21}} \mathrm{M}_{p+q}$$

$$\mathrm{A\cdot} + \mathrm{M}_p^\cdot \xrightarrow{k_{22}} \mathrm{AM}_p$$

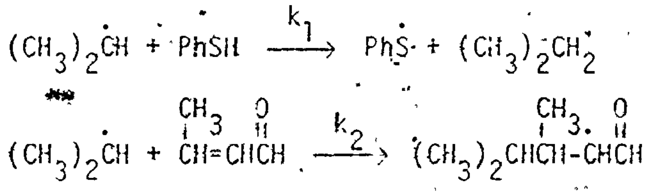
$$\phi\mathrm{O\cdot} + \mathrm{M}_p^\cdot \xrightarrow{k_{23}} \phi\mathrm{OM}_p$$

$$\mathrm{R\cdot} + \mathrm{M}_p^\cdot \xrightarrow{k_{24}} \mathrm{RM}_p$$

increases. In the other case (crotonaldehyde), the yield passes through a maximum as the [olefin] increases. This means an optimum concentration of olefin (i.e., crotonaldehyde) exists, which balances the rates of addition and polymerization, i.e., low concentration means low rate of addition, and high concentration means high rate of polymerization.

Finally, it should be noted that when thiophenol was used instead of phenol, the yields of the adduct decrease drastically (Figure I). This must indicate that the hydrogen-donating ability of thiophenol is much higher than that of phenol, thus nearly all of the isopropyl radicals generated were intercepted by the presence of thiophenol to form propane, and very few of them add to the terminal double bond of the olefin (crotonaldehyde), i.e., $k_1 >> k_2$ in equation [129].

[129]



$$(CH_3)_2\dot{C}H + PhSH \xrightarrow{k_1} Ph\dot{S} + (CH_3)_2CH_2$$

$$(CH_3)_2\dot{C}H + \overset{CH_3}{\overset{|}{C}}H{=}CH\overset{O}{\overset{\|}{C}}H \xrightarrow{k_2} \cdot(CH_3)_2CH\overset{CH_3}{\overset{|}{C}}H-CH\overset{O}{\overset{\|}{C}}H$$

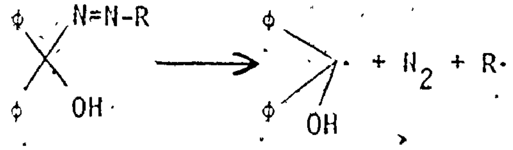
5.2.4 Reactions with Nitrosobenzene in Benzene Solutions

The indirect detection of short-lived radicals by the spin trapping technique is well documented (see section 1.3). In the present work, nitrosobenzene was used as a spin trap to capture the radicals generated from 73. The e.s.r. spectra of the nitroxide radicals, resulting from the reactions of nitrosobenzene and 73 in benzene solutions (degassed) according to equation [16], were taken at room temperature.

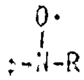
The spectra obtained in all cases are fairly complex (Figures

V, VI, VII, VIII, IX, X and XI). We have not attempted to analyse the spectra completely except in two cases, with R = phenyl, and tert-butyl (Table 10). In other cases, only the a_N and g values of the corresponding nitroxide radicals are reported. The a_N values are about 10-13 gauss (Table 10) in agreement with the range of a_N values for aryl alkyl nitroxide radicals.[38] Besides, the splitting constants (Table 10) are in good agreement with those reported in the literature (Table 11). Therefore, the radicals from 73 that were trapped by nitrosobenzene are alkyl radicals.

It has been reported[236] that diphenylhydroxymethyl radicals are not spin trapped by 2-methyl-2-nitrosopropane but are converted instead to benzophenone by transfer of the hydroxyl hydrogen to the nitroso group. It is clearly indicated in the two well-resolved spectra of nitroxides (Figures V and VI) that no hydrogen atoms were spin trapped by nitrosobenzene. This strongly indicates that 73 decomposes via a radical chain process rather than by unimolecular homolysis of usual azo compounds (equation [130]).

[130] 

The nitroxide radical with R = CH_2CH_2OH (Figure VII) is of considerable interest. There is a possibility of a 'large' splitting by through-space coupling to a single proton, depicted in structure 77. This type of 1,6-interaction in a quasi-six-membered cyclic system has been suggested by Norman[265] to explain the hyperfine splitting in

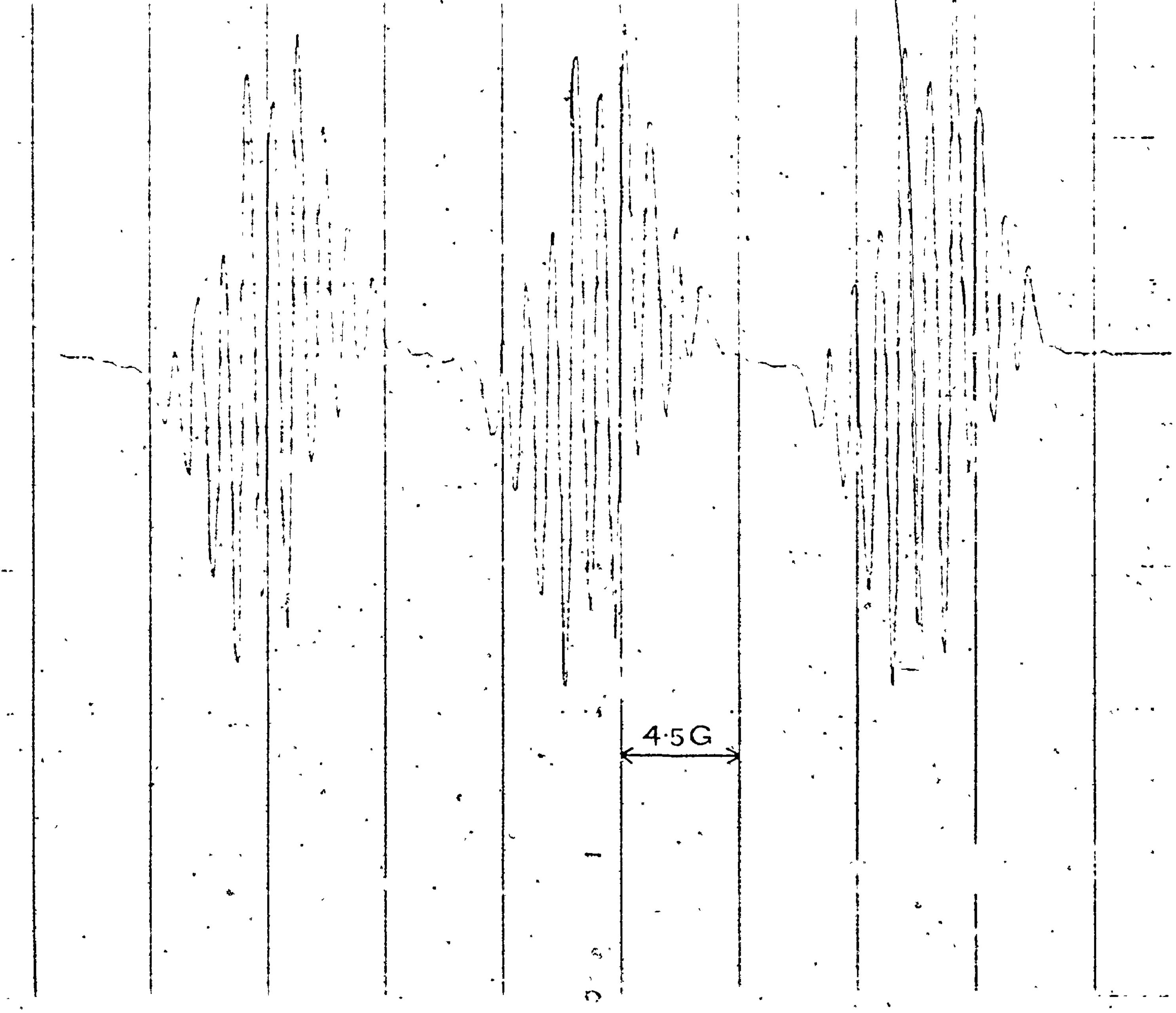
Table 10: The Splitting Constants (gauss) of Nitroxide Radicals  $\phi-\overset{\overset{O\cdot}{|}}{N}-R$

R	a_H	g	Other Splittings
tert-butyl	12.89	2.0071	$a_H^o = a_H^p = 2a_H^m = 1.91$
isopropyl	10.96	2.0064	
ethyl	—	—	
methyl	10.48	2.0067	
phenyl	9.81	2.0057	$a_H^o = a_H^p = 2a_H^m = 1.85$
benzyl	—	—	
allyl	10.4	2.0056	
2-hydroxyl	11.4	2.0059	
cyclohexyl	10.9	2.0072	

Table 11: The Splitting Constants (gauss) of Some Known Nitroxides

Nitroxides	a_N	a_H^o, a_H^p	a_H^m	a_H^β	Ref.
$\phi-\overset{O\cdot}{\overset{\vert}{N}}CH_3$	11.0	2.9	1.0	10.4	260
$\phi-\overset{O\cdot}{\overset{\vert}{N}}CH_2CH_3$	11.1	2.9	1.0	8.3	260
$\phi-\overset{O\cdot}{\overset{\vert}{N}}CH_2CH_3$	11.8	3.2	1.1	9.1	261
$\phi-\overset{O\cdot}{\overset{\vert}{N}}CH(CH_3)_2$	11.1	2.8	0.9	2.8	262
$\phi-\overset{O\cdot}{\overset{\vert}{N}}-C(CH_3)_2$	13.4	1.9	0.8	—	263
$\phi-\overset{O\cdot}{\overset{\vert}{N}}-C(CH_3)_3$	12.4	2.0	0.9	—	42
$\phi-\overset{O\cdot}{\overset{\vert}{N}}-CH_2OH$	11.1	3.0	—	8.0	264
$\phi-\overset{O\cdot}{\overset{\vert}{N}}-\phi$	10.9	1.9	0.9	—	260
$CH_3-\overset{O\cdot}{\overset{\vert}{N}}-CH_2OH$	15.3	$a_H^{CH_3} = 13.3$; $a_H^{CH_2} = 9.5$			260

Fig V The E S R Spectrum of tert-Butyl-Phenylnitroxide



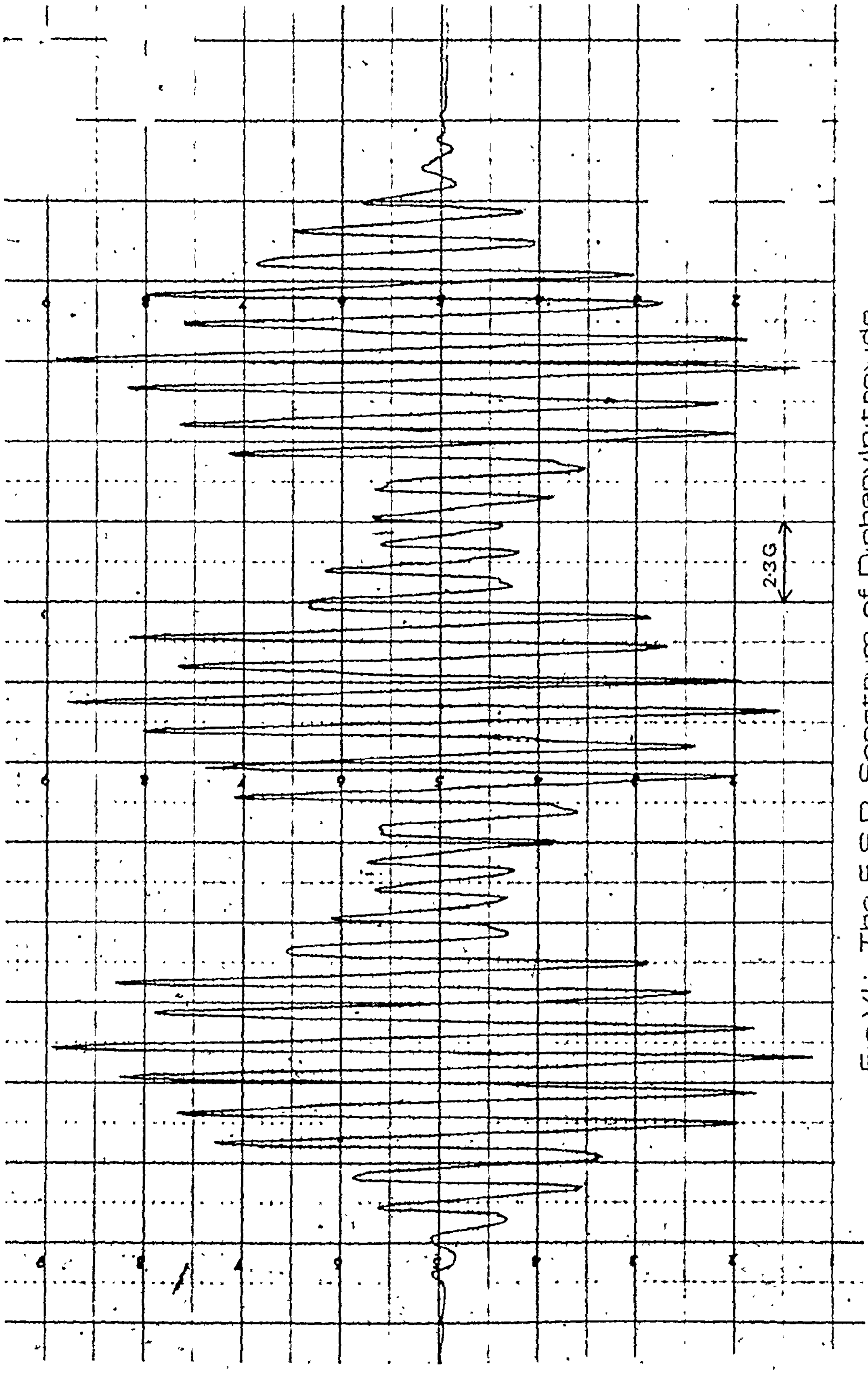


Fig VI: The E.S.R. Spectrum of Diphenylnitroxide

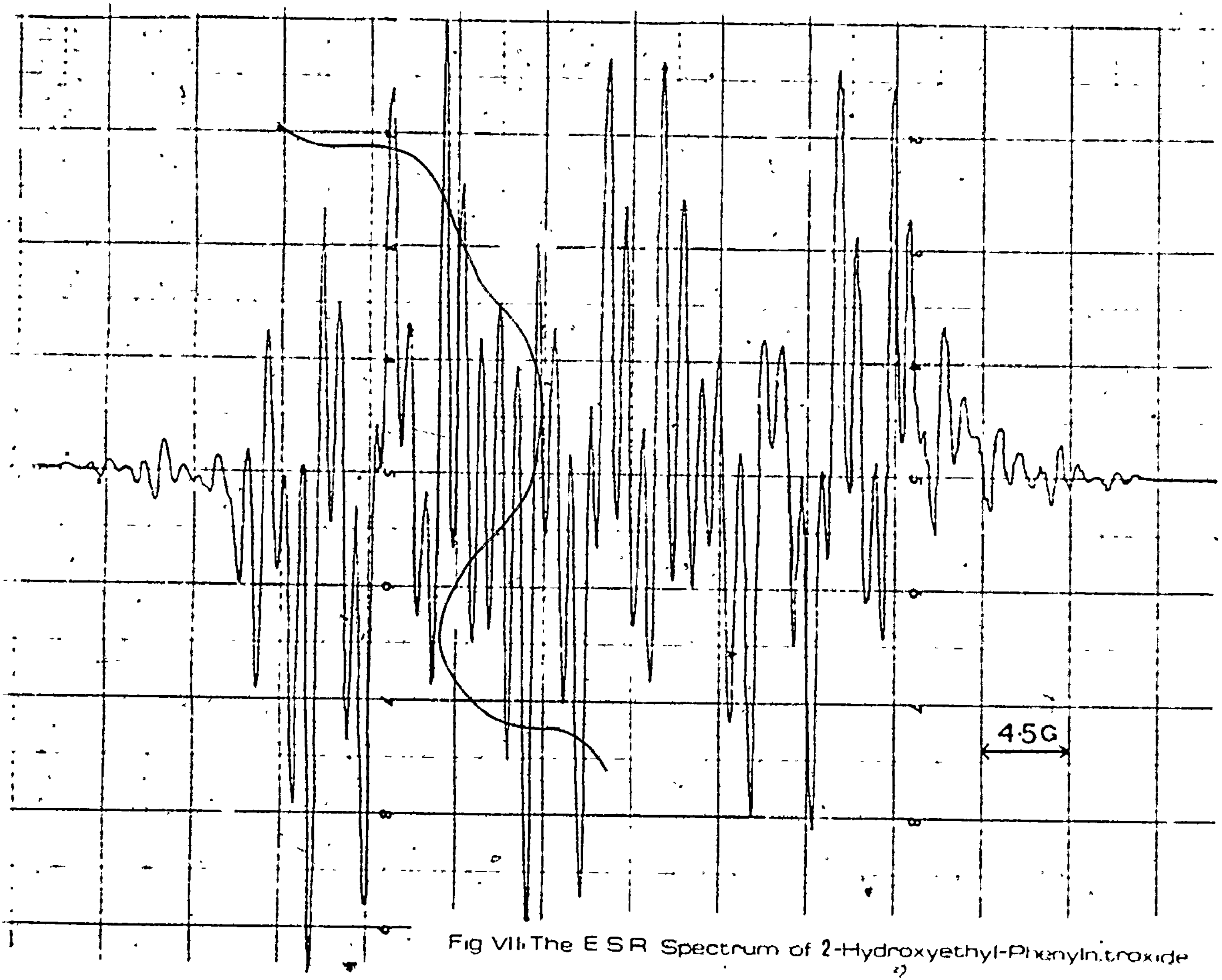


Fig VII. The E S R Spectrum of 2-Hydroxyethyl-Phenylnitroxide

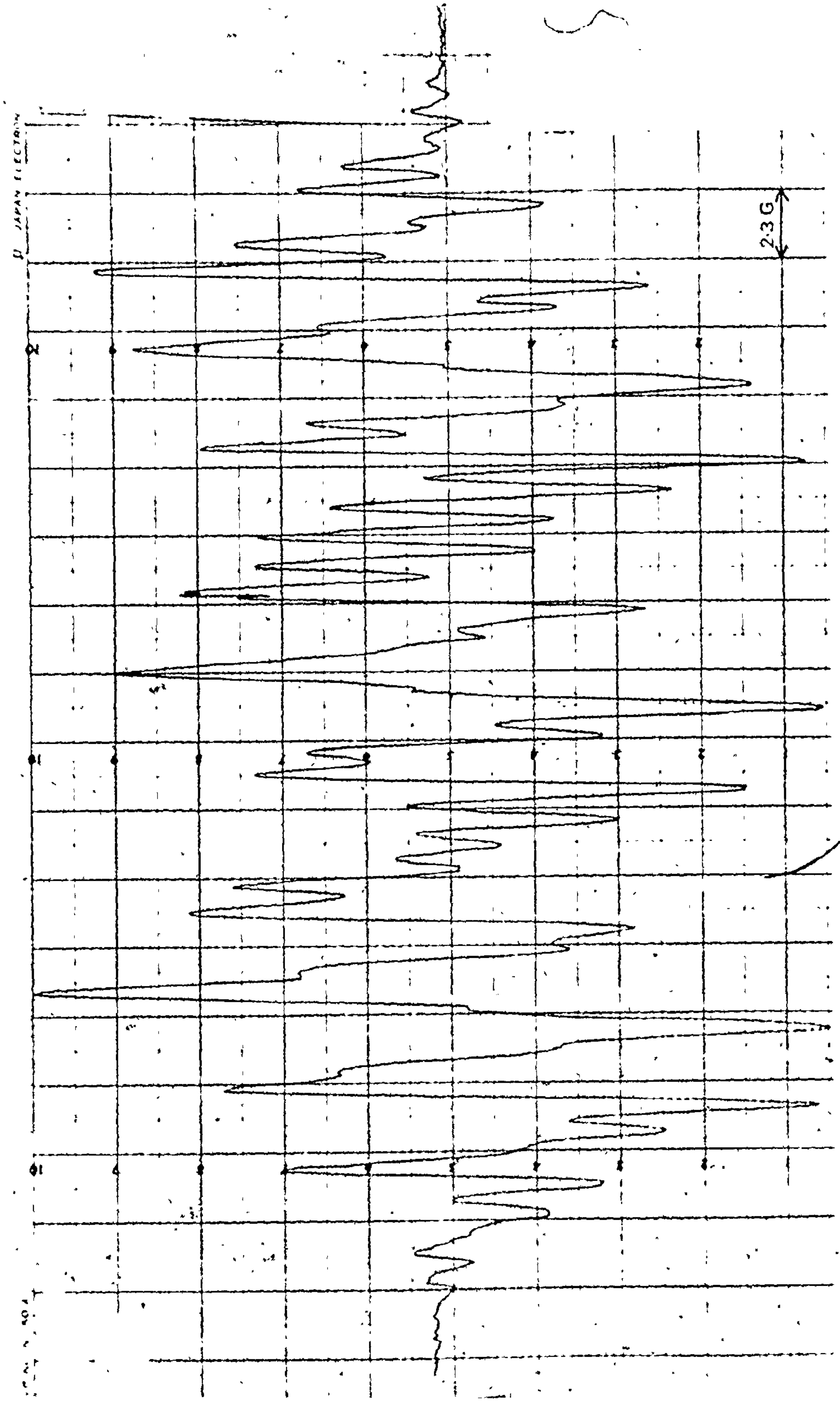


Fig.VIII: The E.S.R. Spectrum of Isopropylphenylnitroxide

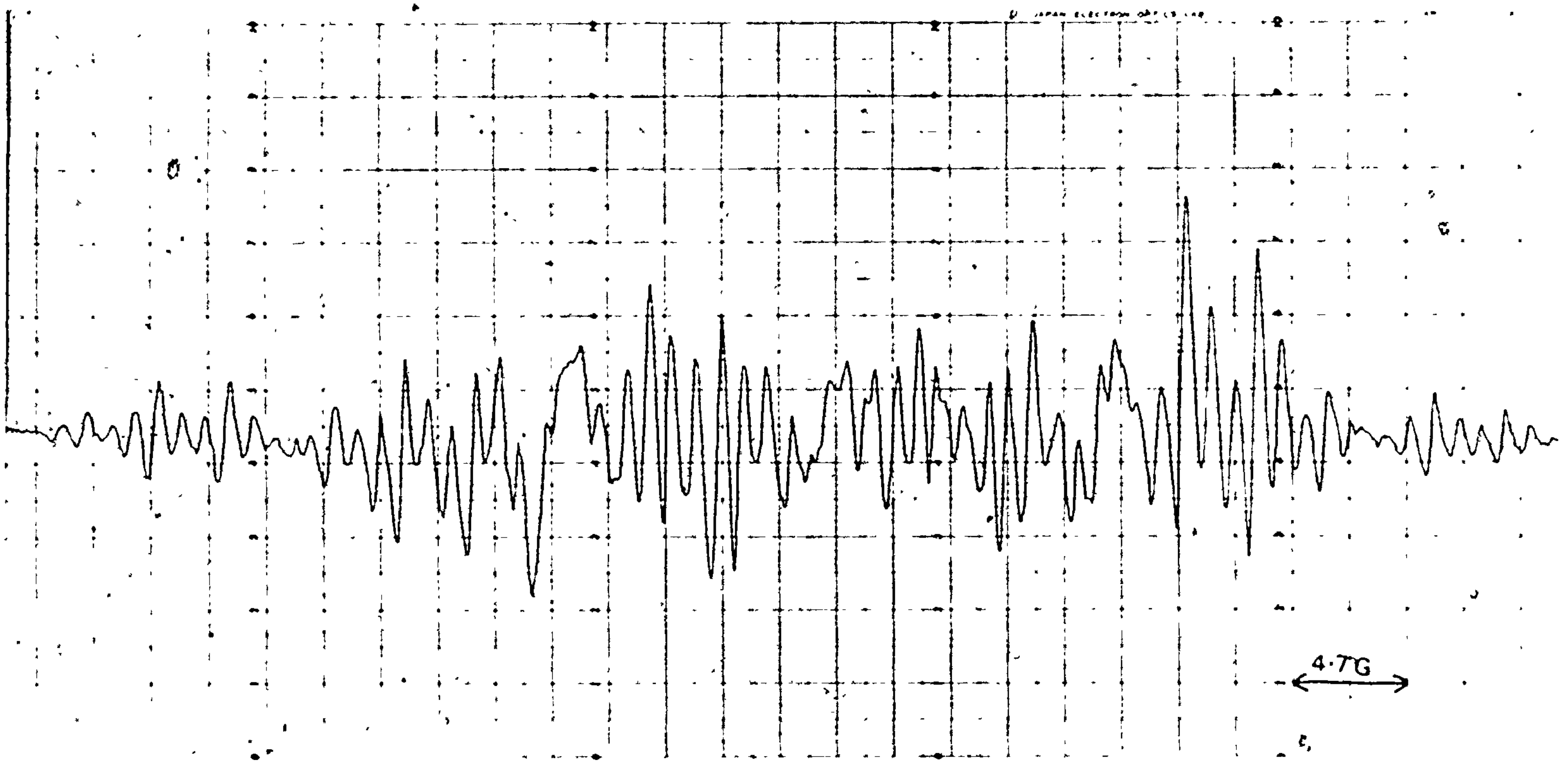


Fig.IX : The E.S.R. Spectrum of Methylphenylnitroxide

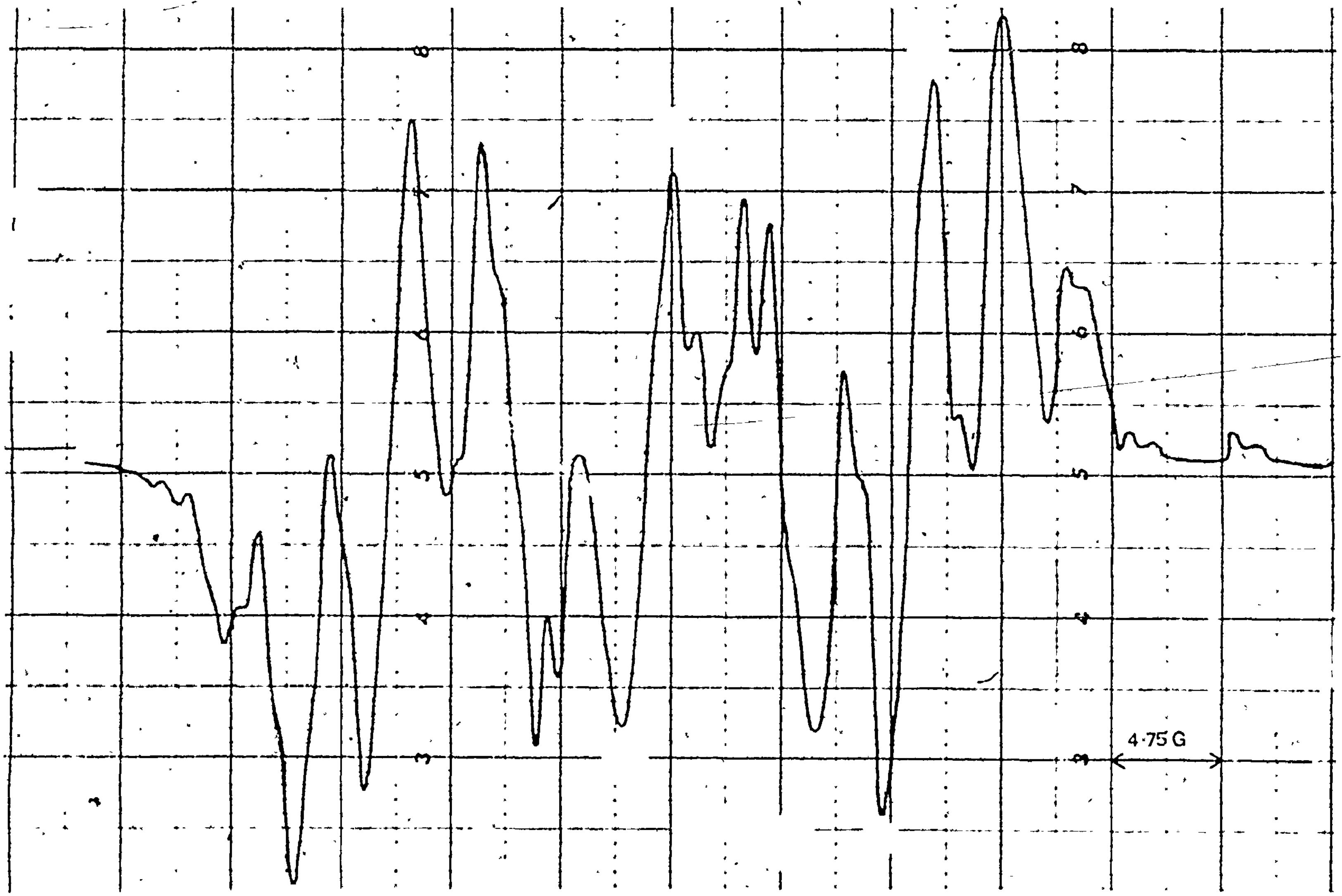


Fig. X: The E.S.R. Spectrum of Allylphenylnitroxide

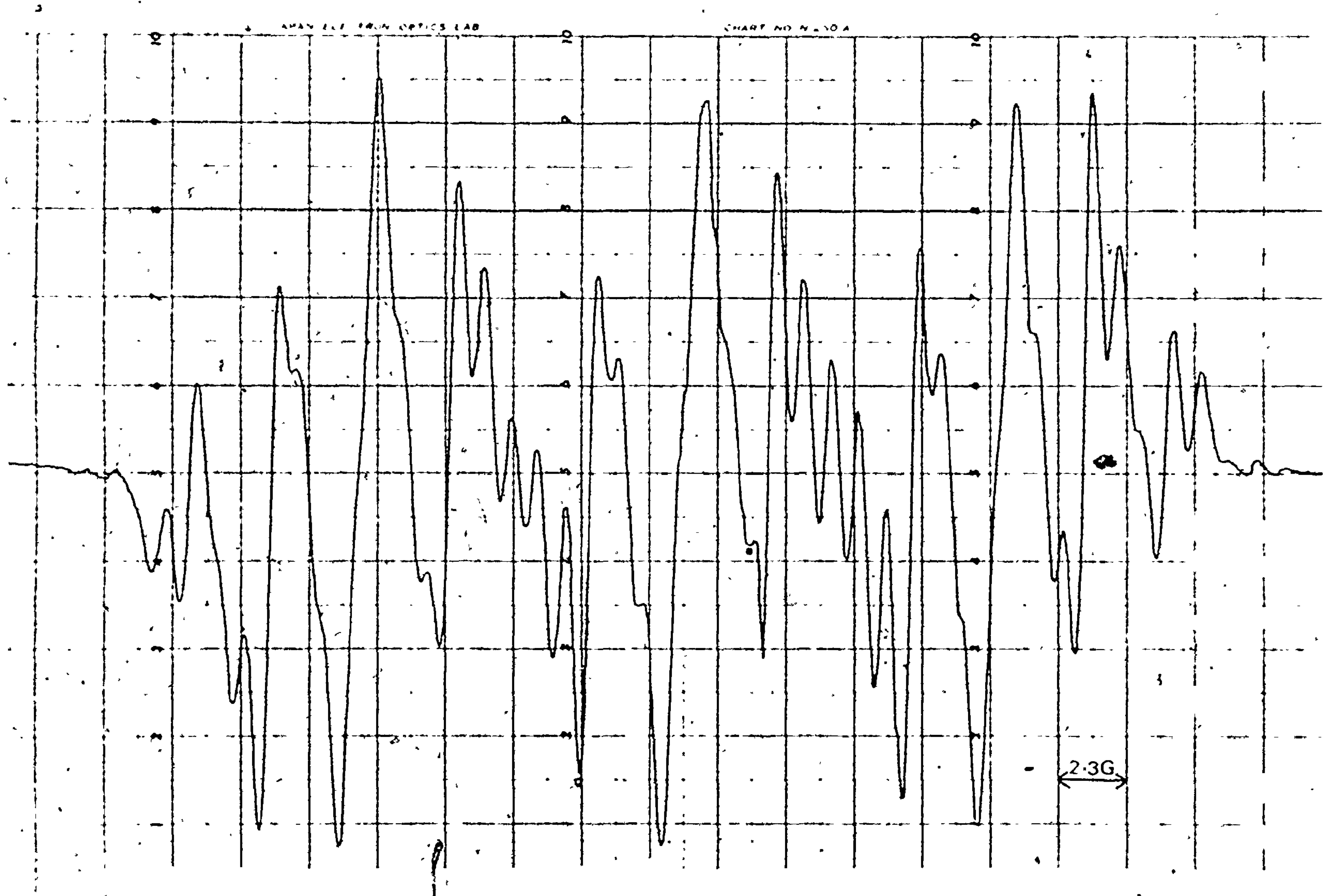
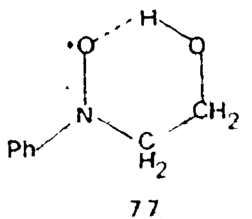
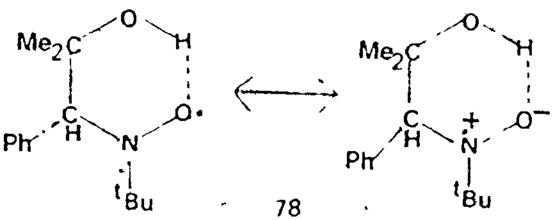


Fig XI: The E.S.R. Spectrum of Cyclohexylphenylnitroxide

certain iminoxy radicals, and by Perkins[53] to explain the appreciably larger nitrogen and β-hydrogen splitting constants of a nitrone spin-adduct 78.


77


78

Inspection of the e.s.r. spectrum of 2-hydroxyethylphenyl nitroxide (Figure VII), however, does not give any evidence for the existence of such hydrogen bonding, even though the spectrum has not been completely analysed. Analogous to this observation, the spectra of $\phi-\overset{O\cdot}{N}CH_2OH$ and $CH_3-\overset{O\cdot}{N}CH_2OH$, reported by Chachaty[264] and Rassat,[265] respectively, did not give any considerable splitting due to the hydroxyl hydrogen (Table 11). Such hydrogen bonding is therefore either unimportant or non-existent.

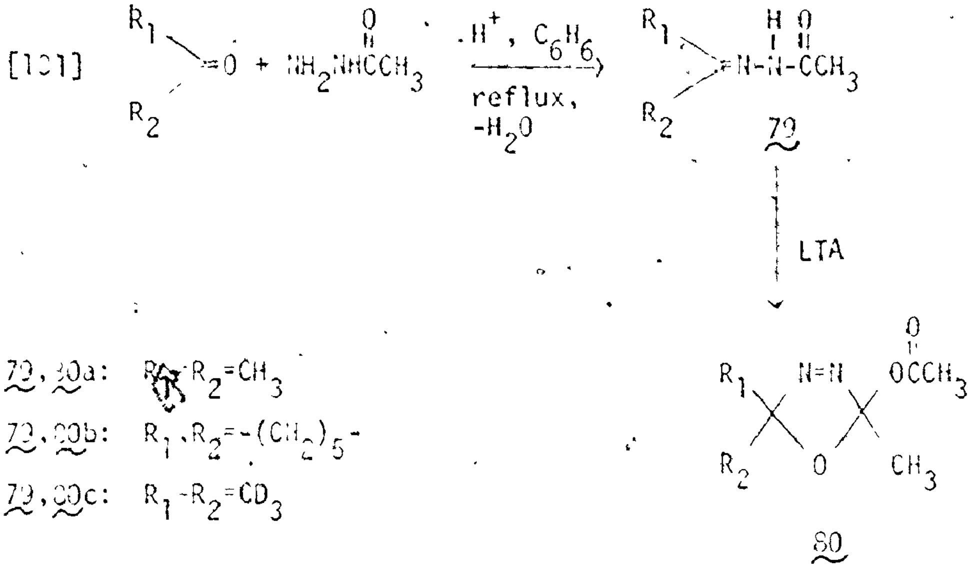
The major significance of the e.s.r. results to the present work is that radical intermediates are indicated in the decomposition of azocarbinols 73.

5.3 Synthesis and Pyrolysis of 2-Acetoxy-2-Methyl-5,5-Dialkyl-Δ^3-1,3,4-Oxadiazolines

5.3.1 Synthesis

The synthesis of Δ^3-1,3,4-oxadiazolines, 80a and 80b, was accomplished by oxidative cyclization of ketone acetylhydrazones, 79a and 79b, respectively, with lead tetraacetate (LTA). Such ketone acetylhydrazones, 79a and 79b, in turn, were prepared by condensation of ketones and acetylhydrazine. The synthetic steps are shown in equation [131].

[101]

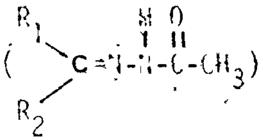


79,80a: $R_1=R_2=CH_3$
79,80b: $R_1,R_2=-(CH_2)_5-$
79,80c: $R_1=R_2=CD_3$

The condensation of ketones and acetylhydrazine was carried out in benzene solution with continuous removal of water, formed in the reaction, by a Dean Stark trap. The yields as well as the spectroscopic data of the acetylhydrazones prepared are gathered in Table 12. A singlet peak near 2.20 is present in the p.m.r. spectra, which is due to the resonance of protons in the acetyl group ($-COCH_3$) of the molecules. A strong band near 1670 cm^{-1} in the i.r. spectra of the hydrazones is assigned to the C=O stretching vibration. The frequencies of the N-H stretching vibration occur near 3200 cm^{-1} in the i.r. spectra. The melting points of the hydrazones reported are in good agreement with those reported in the literature (Table 12).

Compounds 80 were prepared by treatment of 79 with LTA in methylene chloride at 0°C. The yields obtained were about 70-80%. Both compounds 79 and 80 are stable at room temperature for quite a long period. The spectroscopic data of 80 are presented in Tables 13 and 14. The structures of 80 will be discussed in the following section, 5.3.2.

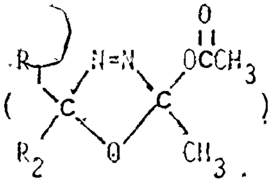
Table 12: Yields and Properties of Acetylhydrazones 79 (



$R_1R_2C{=}N{-}NH{-}C(=O){-}CH_3$)

Compound	Yield	M.P. °C	p.m.r. ($CDCl_3$)	i.r. cm^{-1}	m.s. mol. wt.
$R_1=R_2=CH_3$ acetone-N-acetylhydrazone	90	139.5-140.5 (lit.[266] 139.5-140)	1.87(s,3) 1.97(s,3) 2.20(s,3) 9.50(s,1)	3200,3100,2950,1670, 1400,1370,1340,1250, 1135,1040,1010,865	114
$R_1,R_2=-(CH_2)_5-$ [a] cyclohexanone-N-acetylhydrazone	70	125-126 (lit.[267] 123-124)	1.48-1.92 (m,6) 2.25(s,3) 2.08-2.58 (m,4) 9.75(s,1)	3370,2950,2870,1668, 1490,1445,1430,1370, 1345,1330,1275,1250, 1230,1140,1110,1015 ($CDCl_3$)	154

[a] Elemental analysis calcd. for $C_8H_{14}N_2O$: C 62.29; H 9.16; N 18.18. Found: C 62.44; H 9.13; N 17.93.

Table 13: Properties of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines ()

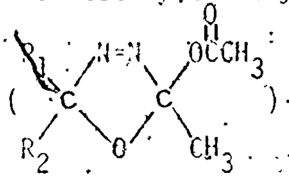
Compound[a]	p.m.r. (CDCl$_3$)	i.r. cm^{-1}	u.v.	n_D^{26}	Analyses
R_1=R_2=CH$_3$	δ1.56(s,6), δ1.92(s,3) δ2.05(s,3) The singlet at δ1.56 was split into two singlets in CCl$_4$; C$_6$H$_6$ or nitrobenzene as solvent.	2995,2940,1760,1460, 1435,1385,1370,1225, 1200,1130,1110,1010, 985,920	λ_{max}=313.8 nm ε = 199	1.4200	$C_7H_{12}N_2O_3$ Calcd. Found C:48.81 49.21 H: 7.03 6.99 N:16.27 16.00
R_1,R_2=-(CH$_2$)$_5$-[b]	δ1.43-2.20(m,10) δ1.94(s,3) δ2.04(s,3)	2945,2860,1755,1575, 1445,1365,1265,1245, 1230,1180,1140,1120, 1080,1010,975 (CDCl$_3$)	λ_{max}=317.4nm ε = 185	1.4560[c]	$C_{10}H_{16}N_2O_3$ Calcd. Found C:56.57 56.29 H: 7.60 7.71 N:13.21 12.95

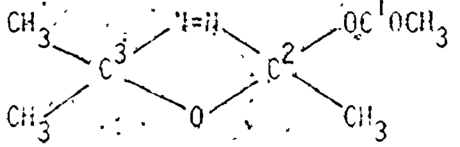
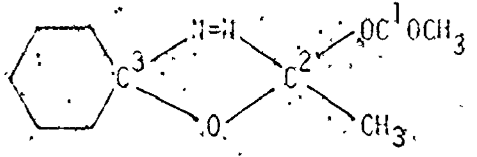
[a] The mass spectra all showed m/e = M-28 peak due to loss of nitrogen.

[b] The compound melted at 28.5-30.5°C.

[c] The refractive index was taken immediately after it melted at room temperature.

Table 14: ^{13}C Chemical Shifts (ppm) of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines 80

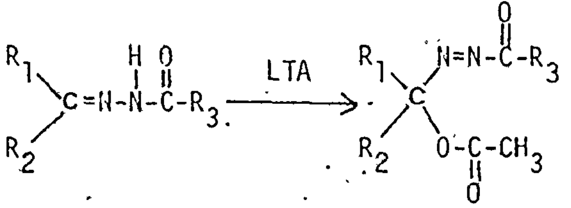


R	Structure	C^1	C^2	C^3	The remaining carbons
$R_1=R_2=CH_3$		167.7	130.1	123.8	24.8,23.9,23.0,21.7
$R_1,R_2=-(CH_2)_5-$		167.5	129.1	125.5	34.6,33.7,24.9,23.1,21.7

Deuterium labelled compounds, 79c and 80c, were prepared in the same way (equation [131]) resulting in 96 atom % D incorporated as estimated by mass spectrometry[258] and p.m.r. analysis.[268] The deuterium content of 80c was estimated from the fragment $[M-28]^+$, formed by loss of nitrogen, in the mass spectrum.

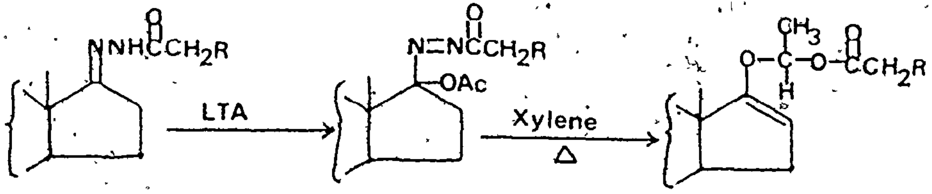
5.3.2 Structures

Reactions of LTA with ketone carbonylhydrazones of type 79 might be expected to give acyclic azoacetates 81 (equation [132]). In fact,

[132] 

81

it had been reported by Iffland[269] (equation [132] with $R_{1,2}$ or R_3 = alkyl), and by Pitt[270] (equation [133]) that azoacetates were isolated in stable form. However, it has been shown in the present work that their structure assignments were in error. Pitt had studied the pyrolysis of what he called 82 in xylene, and high yields of enol ethers 83 were obtained (equation [133]). Quite understandably, Pitt had difficulty in accounting for the result mechanistically because he never had 82 to begin with.

[133] 

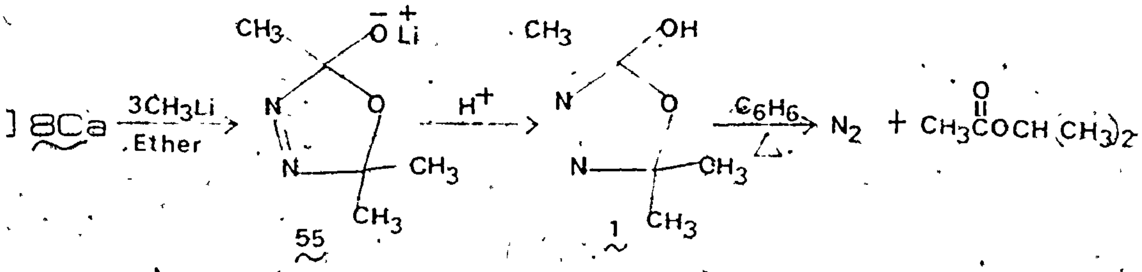
82 83

The presence of an acetate group in 80 is shown clearly both by p.m.r. (a singlet near δ 2.00) and by i.r. (a strong band near 1755 cm^{-1}). The ultraviolet spectrum of 80 shows a λ_{max} near 313 nm with extinction coefficient about 200 (Table 13). This is due to the $n\to\pi^*$ absorption of the azo (N=N) function presented in the molecule. The values of λ_{max} of 80 are in good agreement with those reported by Pitt[270] for what he called compound 82.

The cyclic nature of 80 was confirmed both by ^{13}Cmr spectroscopy and by their chemical reactivities. Two quarternary carbons and only one carbonyl carbon were observed in ^{13}Cmr spectra of both 80a and 80b (Table 14). In contrast, acyclic azoacetates 81 have two carbonyl carbons and only one quarternary carbon.

Treatment of 80a with methyl lithium (3-fold excess) in ether at 0°C, and subsequent acidification with NH_4Cl solution gave 1 which decomposed fairly cleanly to isopropyl acetate in benzene solution (equation [134]). The lithium salt 55 can be isolated and kept in a

[134]



refrigerator for ~~quite~~ a long time without decomposition. The experimental results were in complete agreement with those reported by Knittel and Warkentin[20,171] on independently prepared compounds 55 and 1. The acyclic azoacetate 81, under the same conditions, could not give isopropyl acetate by any conceivable mechanisms. Moreover, the products from the thermolysis of 80a and 80b can also be explained satisfactorily in terms of a cyclic structure (see section 5.3.6).

5.3.3 Mechanism of Oxidative Cyclization

A mechanism for the observed oxadiazoline formation must take into account studies by other workers on LTA oxidation of ketone carbonylhydrazones (see page 43). The oxidation of benzoyl hydrazones to 2-acetoxy-Δ^3-1,3,4-oxadiazolines, recently reported by Hoffmann[198-201] and by Norman,[189] is the most closely related to the reactions reported here. Different polar mechanisms have been suggested by each worker, as shown in equations [85] and [112]. The mechanism proposed by Hoffmann required elimination of acetic acid from an initially formed intermediate, azoacetate. Such an uncatalyzed elimination would not be expected to be rapid at low temperature. Moreover, the evidence for the existence of the azoacetate as the intermediate was weak and inconclusive, since the compound was nonisolable.

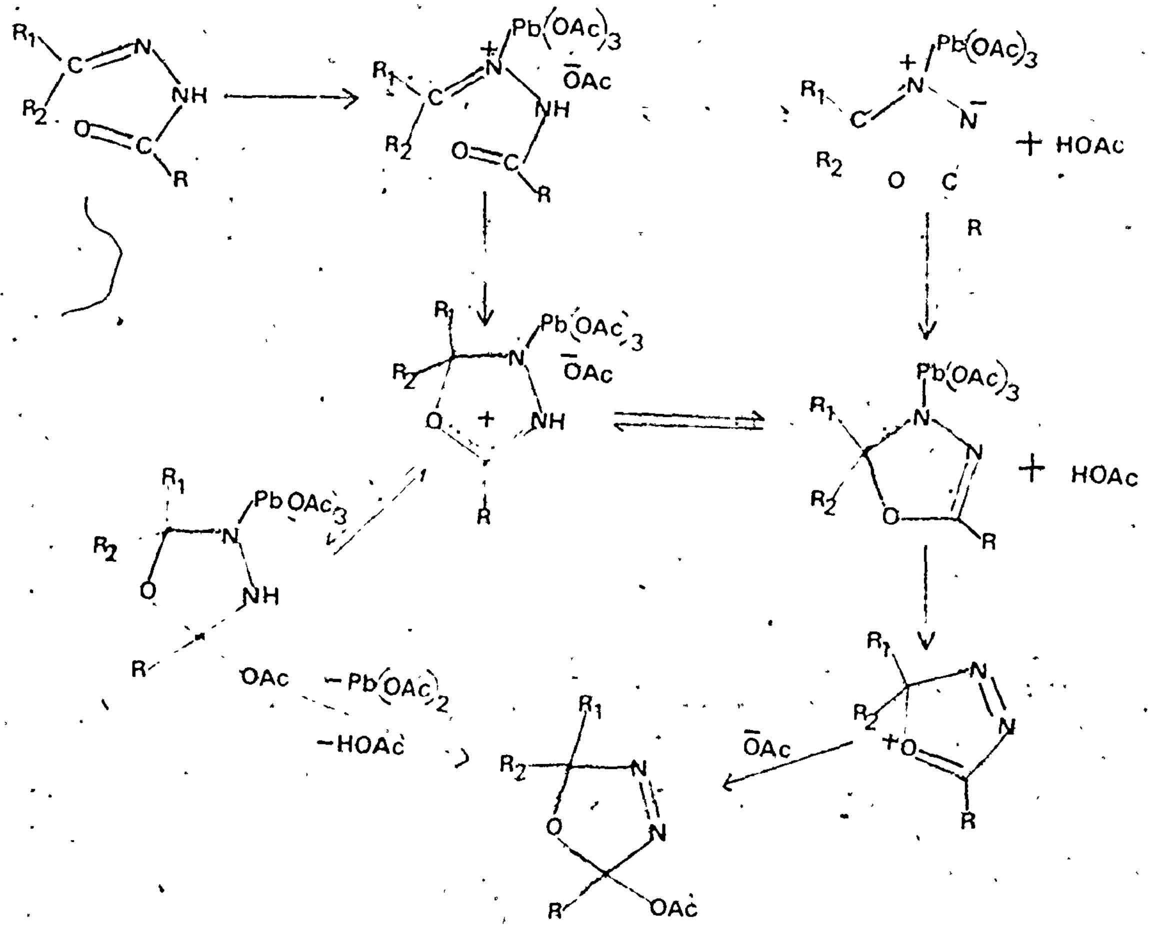
The mechanism proposed by Norman[189] seems more attractive. Following intramolecularly promoted decomposition of the hydrazone-lead complex, the resulting cation was attacked by an acetate ion leading to oxadiazoline 63. Norman assigns the oxonium ion mechanism on the evidence that in methanolic solution, a methoxy group rather than an acetate group is incorporated into the oxadiazoline 63.

In addition to the mechanism of the formation of oxadiazolines proposed by Norman, an alternative mechanism may be suggested, as depicted in equation [135].

5.3.4 Pyrolysis of Oxadiazolines

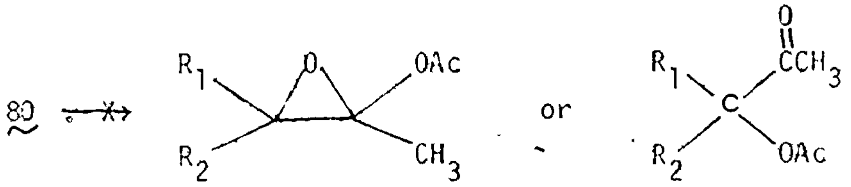
Hoffmann[198-201] has studied the pyrolysis of oxadiazolines 63, and found that 63 decomposed to the epoxyacetates 65 which gave the α-

[135]



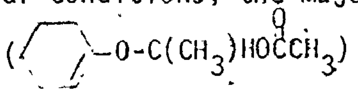
acetoxy ketone 66 upon heating (equation [113]). The decomposition of 63 to 65 was explained by postulating a carbonyl-ylide intermediate 64, formed by loss of nitrogen, which subsequently closed to give 65. The existence of 64 was confirmed by trapping experiments with norbornene and dimethylacetylenedicarboxylate (see page 59).

However, upon pyrolysis of 80 in benzene at the boiling point in air for two days, the products obtained were completely different from that expected; neither epoxyacetate nor α-acetoxy ketones were formed (equation [136]). Similar results were obtained when the pyrolysis was done in carbon tetrachloride, chlorobenzene or nitrobenzene at 80°C in air for 48 hours.

[136] 

On thermolysis of 80a, the following five products were isolated with glpc. The bracketed number is the yield of the product. They are acetone 84 (trace), acetic anhydride 85 (5%), 1,1-diacetoxyethane 86 (4%), 2,2-diacetoxypropane 87 (2%) and 1-acetoxyethyl-2-propenyl ether ($CH_2=C(CH_3)-O-C(CH_3)HO\overset{O}{C}CH_3$) 88 (87%).

Acetone 84 was identified by comparing its retention times on several glpc columns with those of an authentic sample. The remaining four products were identified by their spectroscopic data and analysis (Table 15). Products 84 to 87 can be accounted for as the secondary products from 88 reacting with a trace of water during the reaction time. Thermolysis of 80a in the presence of anhydrous Na_2SO_4 resulted in approximately 2-fold reduction in the yields of the products 84 to 87. The result of this experiment was taken as evidence for the origin of products 84 to 87, as secondary products from 88.

Under similar conditions, the major product 2-acetoxyethyl-1-cyclohexenyl ether ( $-O-C(CH_3)HO\overset{O}{C}CH_3$) 89 (90%) and one minor product acetic anhydride 85 (3%) were formed, and isolated with glpc, from the decomposition of 80b. No attempt was made to isolate all the other minor products (1-5%) formed in the course of the thermolysis. The spectroscopic data and analysis results of 89 are in Tables 15 and 16.

The structures of the enol-ethers 88 and 89 were established from the spectroscopic data (Tables 15 and 16). The bands near 1735, 1670, and 1240 cm^{-1} are present in the i.r. spectra of 88 and 89. These

Table 15: The Spectroscopic Data of the Products of Thermolysis of 80

Compound	p.m.r.[a] ($CDCl_3$)	i.r. ($CDCl_3$)	m.s. mol. wt.	n_D^{26}	Analysis
Acetic anhydride[b]	δ2.22(s)	1838,1755,1430,1368, 1225,1130,1045,1000	—	—	—
1,1-Diacetoxyethane	δ1.48(d,3,J=6Hz),δ2.07(s,6) δ6.93(q,1,J=6Hz)	3010,2950,1760,1450, 1430,1365,1360,1255, 1220	146	—	—
2,2-Diacetoxypropane[d]	δ1.78(s,6),δ1.98(s,6)	3000,2950,1760,1735, 1650,1430,1370,1260, 1245,1200,1140,1070, 1045,1010,835	—	—	—
1-Acetoxyethyl-2-propenyl ether[e]	δ1.50(d,3,J=6.0Hz) δ1.85(d,3,J=1.0Hz) δ2.08(s,3) δ4.05(m,2,J_1=4.0Hz,J_2=1.0Hz) δ6.07(q,1,J=6.0Hz)	3000,2960,2945,2930, 1735,1670,1640,1450, 1435,1400,1365,1280, 1240,1160,1140,1070, 1020,975,820	144	1.4095	$C_7H_{12}O_3$ Calcd. Found C:58.30 58.36 H: 8.39 8.26
1-Acetoxyethyl-1-cyclohexenyl ether	δ1.41(d,3,J=6.0Hz) δ1.50-1.80(m,4) δ2.00(s,3) δ1.90-2.33(m,4) δ4.73(m,1)δ6,24(q,1,J=6.0Hz)	3000,2940,2870,2850, 1745,1675,1450,1435, 1400,1375,1340,1270, 1240,1180,1170,1155, 1145,1125,1085,1060, 1005,935,920,850 (using CCl_4 as solvent)	184	1.4517	$C_{10}H_{16}O_3$ Calcd. Found C:65.17 64.56 H: 8.76 8.61

[a] The p.m.r. spectra of 2,2-diacetoxypropane and 1-acetoxyethyl-1-cyclohexenyl ether were obtained by using CCl_4 as solvent.

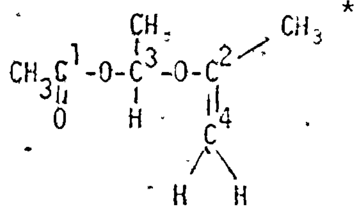
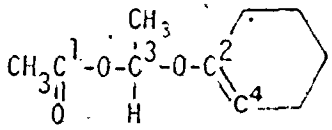
[b] Both p.m.r. and i.r. spectra match those of the authentic sample.

[c] Both p.m.r. and i.r. spectra are in good agreement with those reported in the literature.[271]

[d] The p.m.r. spectrum matches that reported by J.W. Scheeren and coworkers.[272]

[e] In a decoupling experiment, irradiation at δ1.50 turned the quartet at δ[illegible]47 into a singlet. When irradiating at δ1.85, the multiplet at δ4.05 became an AB quartet (J_1= 4.0Hz).

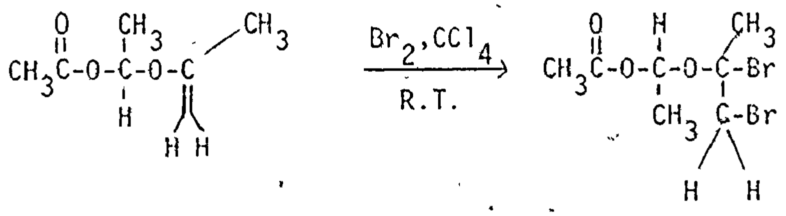
Table 16: ^{13}C Chemical Shifts (ppm) of Enol Ethers 88 and 89

Structure	C^1	C^2	C^3	C^4	The remaining carbons
 *	170.0	156.8	92.6	85.6	20.9,20.7,20.3
	170.0	152.2	99.9	92.3	27.3,23.6,22.8,22.4,21.2,20.7

* With ORCWD (off resonance continuous wave decoupling), the peaks at $\delta_{^{13}C}$ 170.0, 156.8, 92.6 and 85.6 were split into a quartet, a multiplet, and a doublet of quartets, respectively.

bands are due to the stretching modes of C=O, O-C=C and $OCOCH_3$ of the enol ether molecules, respectively. The presence of the acetoxy group, vinyl protons, and the acetal proton of the $-O-\overset{H}{\underset{Me}{C}}-O-$ linkage is clearly indicated in the p.m.r. spectra (Table 15) near δ 2.00, δ 4.00-4.73 and δ 6.00-6.24, respectively. The ^{13}Cmr spectra, together with the assignment, are in Table 16.

The presence of unsaturation in the product 88 was also shown by its ready reaction with bromine in CCl_4 at room temperature. The dibromide was formed (equation [137]); the existence of such a dibromide was observed by p.m.r. (see Experimental, page 168). Shaking the dibromide solution in CCl_4 with a few drops of water at room temperature for one hour gave acetic acid, acetaldehyde and bromoacetone as the major products (equation [138]).

[137]


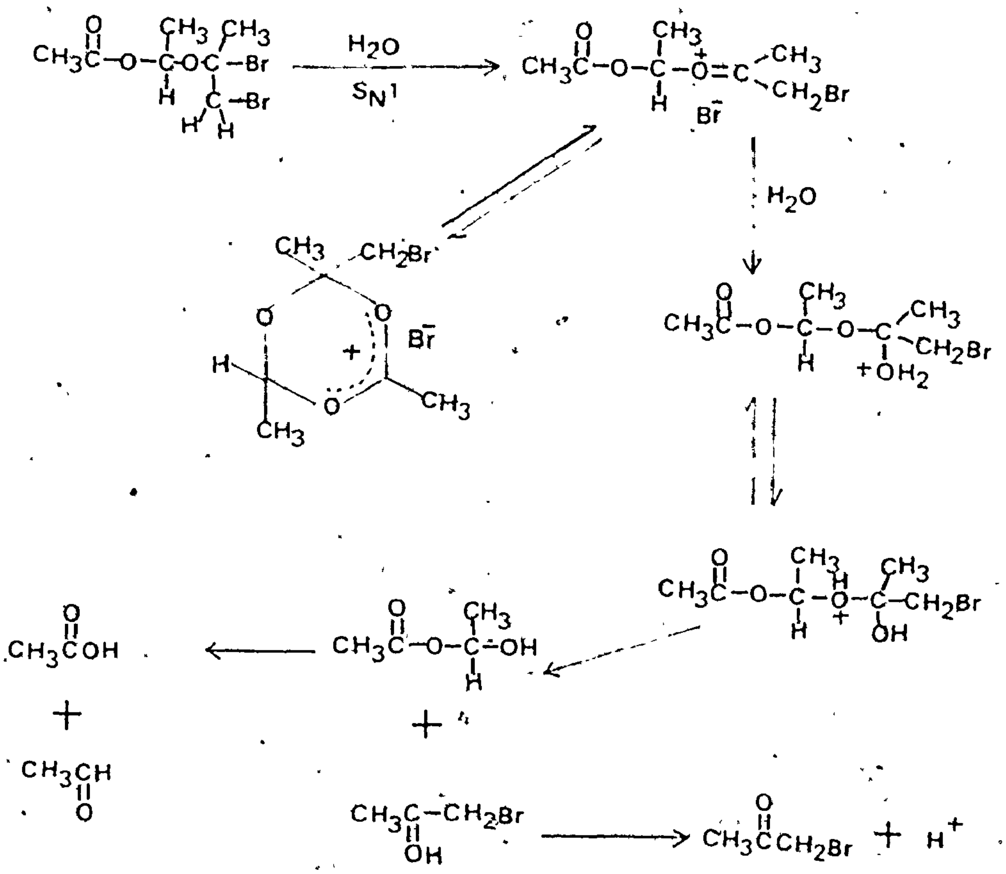
$$CH_3\overset{O}{\overset{\|}{C}}-O-\underset{H}{\overset{CH_3}{C}}-O-\overset{CH_3}{C}=CH_2 \xrightarrow[R.T.]{Br_2,CCl_4} CH_3\overset{O}{\overset{\|}{C}}-O-\underset{CH_3}{\overset{H}{C}}-O-\overset{CH_3}{\underset{CH_2Br}{C}}-Br$$

Under the same conditions, rapid decolourization of bromine was also observed when the enol ether 89 was used instead of 88. However, there was no corresponding dibromide indicated in the resulting p.m.r. spectrum. The failure to detect it might be due to the thermal instability of the expected dibromide.

5.3.5 Kinetics of Thermolysis

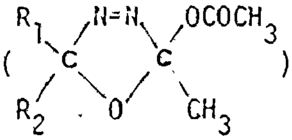
The decompositions of 80a and 80c at 79°C in benzene (and in

[138]



nitrobenzene) solutions (degassed) were followed by p.m.r. spectroscopy using anisole as an internal standard for peak height measurement. The kinetic results are collected in Table 17.

The data of Table 17 show that 80a decomposed with first-order kinetics in both solvents. The decomposition rate constant at two different concentrations of 80a remains fairly constant, within experimental error. This indicates that there was no induced decomposition. Pyrolysis of 80a was independent of solvent polarity, since 80a decomposed both in benzene and in nitrobenzene solutions with comparable rate, within experimental error. Therefore, it can be concluded that no charge or

Table 17: Kinetics of Decomposition of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines 80 () at 79°C

R[a]	Solvent[b]	Initial Concentration M	$k \times 10^5$ $\sec^{-1}$ [c]	Correlation Coefficient
$R_1=R_2=CH_3$	Benzene	0.639	1.22 ± 0.03	0.991
		0.639	1.27 ± 0.02	0.998
		0.262	1.25 ± 0.03	0.989
$R_1=R_2=CH_3$	Nitrobenzene	0.639	1.05 ± 0.02	0.997
		0.262	1.07 ± 0.02	0.995
$R_1=R_2=CD_3$	Benzene	0.618	1.24 ± 0.01	0.999
		0.253	1.26 ± 0.01	0.999

[a] The products were the same except for the labelling with deuterium.

[b] The values of E_T, empirical parameters of the polarity of solvents, of benzene and nitrobenzene are 34.5 and 42.0 kcal $mole^{-1}$, respectively.[273]

[c] The k_H/k_D ratio is 1.00 ± 0.03.

very little charge was developed in the transition state in the course of decomposition of 80a.

The k_H/k_D ratio was found to be 1.00 · 0.03 which shows that there was no primary deuterium isotope effect operating on the present thermolysis. Whether or not there was a secondary deuterium isotope effect is not certain, since the kinetic measurements by p.m.r. spectroscopy are not precise enough to probe this question.

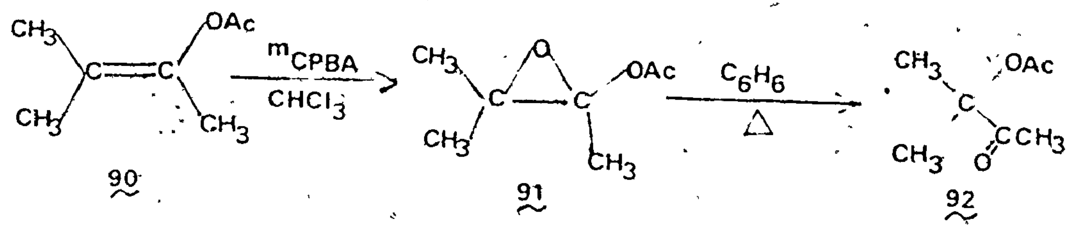
5.3.6 Mechanism of Decomposition

There are several reasonable pathways, depicted in Scheme XI, of opening the five-membered ring of 80a leading to the major product 88. This mechanistic scheme is also applied to the decomposition of 80b.

Path a can be eliminated based on several observations.

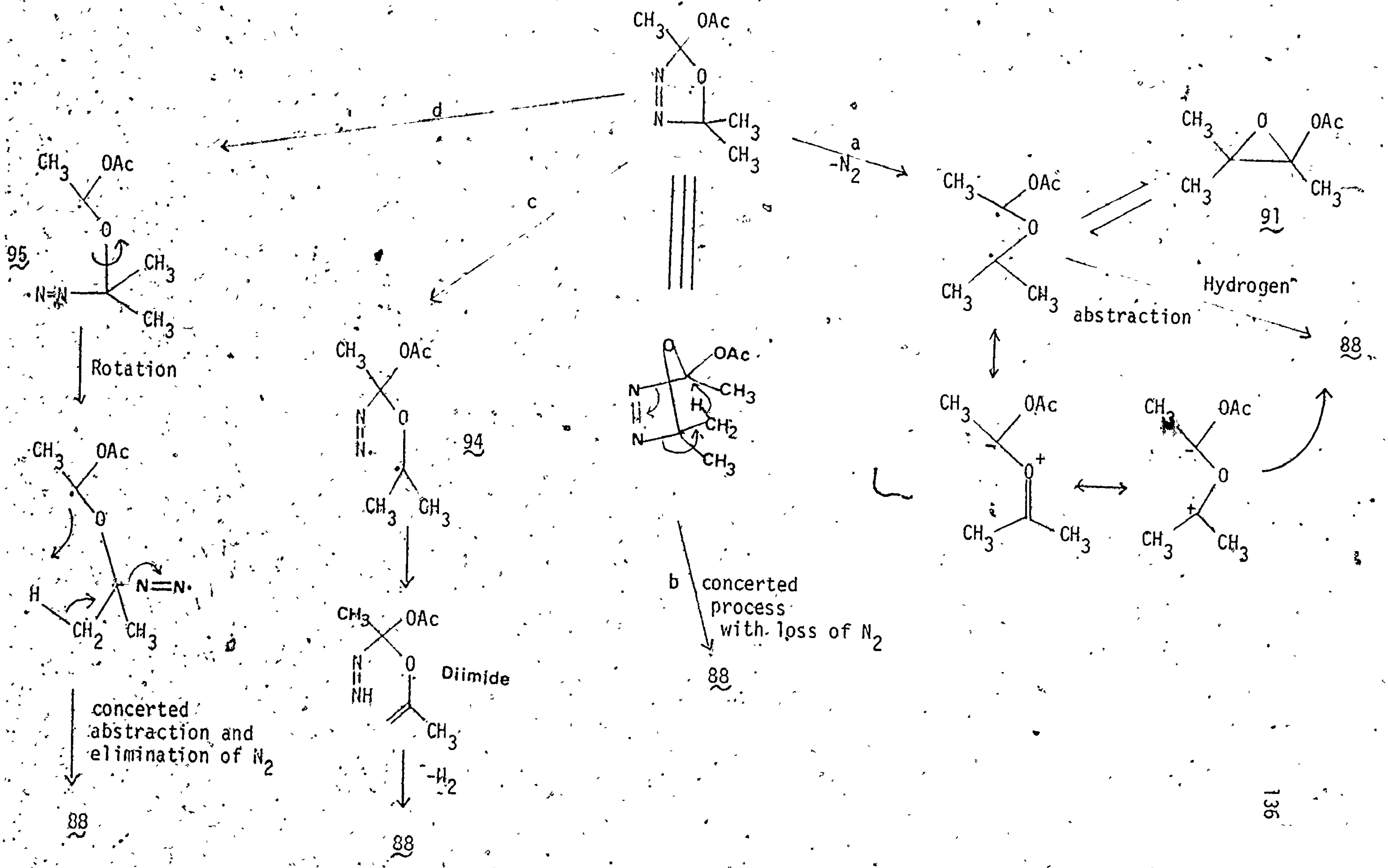
(i) The authentic sample of epoxyacetate 91, prepared by epoxidation of 2-acetoxy-3-methylbut-2-ene 90 with m-chloroperbenzoic acid in chloroform, rearranged nearly quantitatively to acetoxy ketone 92, under the same thermolysis conditions (equation [139]). This thermal rearrangement

[139]



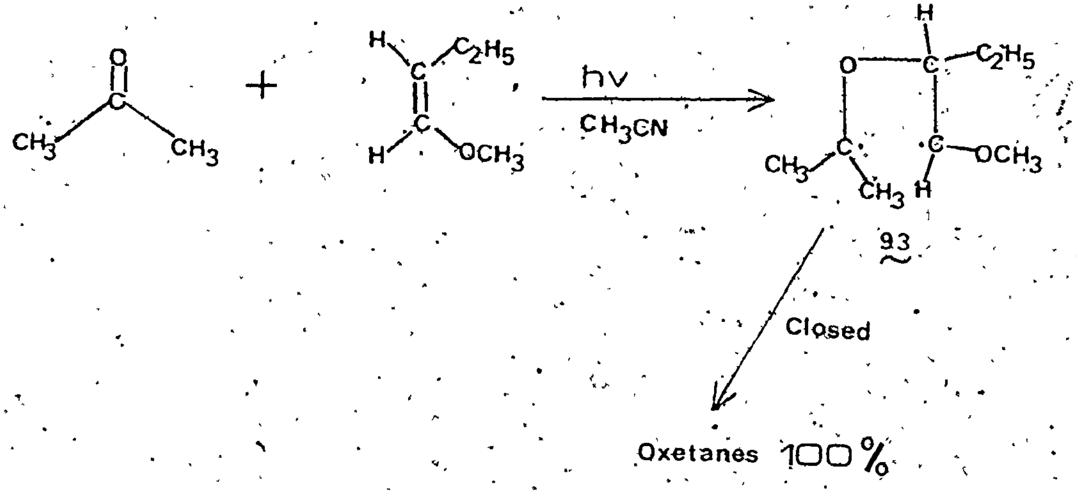
is analogous to rearrangements of other types of epoxyacetates reported by Gardner[274] and by Shine.[275] Therefore, the epoxyacetate 91 was not involved as an intermediate in the course of thermolysis of 80a.

Scheme XI


CH3
OAc
N
O
CH3
d
a
-N2
c
95
N=N
Rotation
94
N=N•
H
CH2
concerted abstraction and elimination of N2
88
Diimide
NH
-H2
b
concerted process with loss of N2
91
Hydrogen abstraction

(ii) It was found that the decomposition rate of 80a is independent of the solvent polarity (see previous section). Hence, the involvement of a carbonyl-ylid as an intermediate was ruled out, in contrast to the pyrolysis of 63, in which the carbonyl-ylid 64 was suggested as an intermediate.

(iii) Turro and coworkers[276,277] suggested a diradical intermediate 93 in the photochemical reaction of acetone with 1-methoxy-1-butene in acetonitrile. Such diradical 93 will close with 100% yield to form oxetanes (equation [140]). This diradical intermediate 93 can act as

[140] 

a model for our case. Therefore, there is probably no diradical intermediate formed during pyrolysis of 80a; otherwise, it should have closed to give the epoxyacetate 91 or its decomposition product, acetoxy ketone 92. However, no trace of 91 or 92 was detected from thermolysis, and also from photolysis (300 nm, 0°C) of 80a in chlorobenzene.

Path b was ruled out simply based on the fact that there is no primary deuterium isotope effect operating in the course of thermolysis (see section 5.3.5). Thus, the hydrogen abstraction or shift is not part of the rate determining step. Also, the molecule has to be in a suitable conformation for such a hydrogen shift to occur, with concerted loss of molecular nitrogen. The molecule in such a conformation might encounter steric constraints.

The remaining two paths, c and d, involve the stepwise cleavage of the oxadiazoline ring, in the rate determining step. Path c involves the initial rupture of N-C_5 bond. There are two possible subsequent reactions for the resulting diazenyl radical 94. It can either undergo intramolecular hydrogen abstraction via a seven-membered cyclic transition state to give a diimide which then loses nitrogen[12] to yield 88, or give off nitrogen to form a diradical that was postulated as intermediate in path a. However, we have discussed earlier that such a diradical (in path a) could not have participated in the course of pyrolysis of 89a. Besides, it is known that reactions via a seven-membered cyclic transition state are normally not facile compared with those via five- or six-membered transition states. Consequently, the intramolecular hydrogen abstraction would not be expected to be fast and efficient enough to compete with loss of N_2.

Path d consists of breaking the N-C_2 bond in the rate determining step. Immediately following rotation about the O-C bond of the resulting diradical 95 and intramolecular abstraction of hydrogen with concerted elimination of nitrogen are suggested. The hydrogen abstracting step involves a five-membered cyclic transition state, and it is also assisted by a driving force due to the heat of formation of nitrogen. Therefore, the intramolecular abstraction of hydrogen might be expected to be very fast and efficient enough to compete with unassisted loss of N_2.

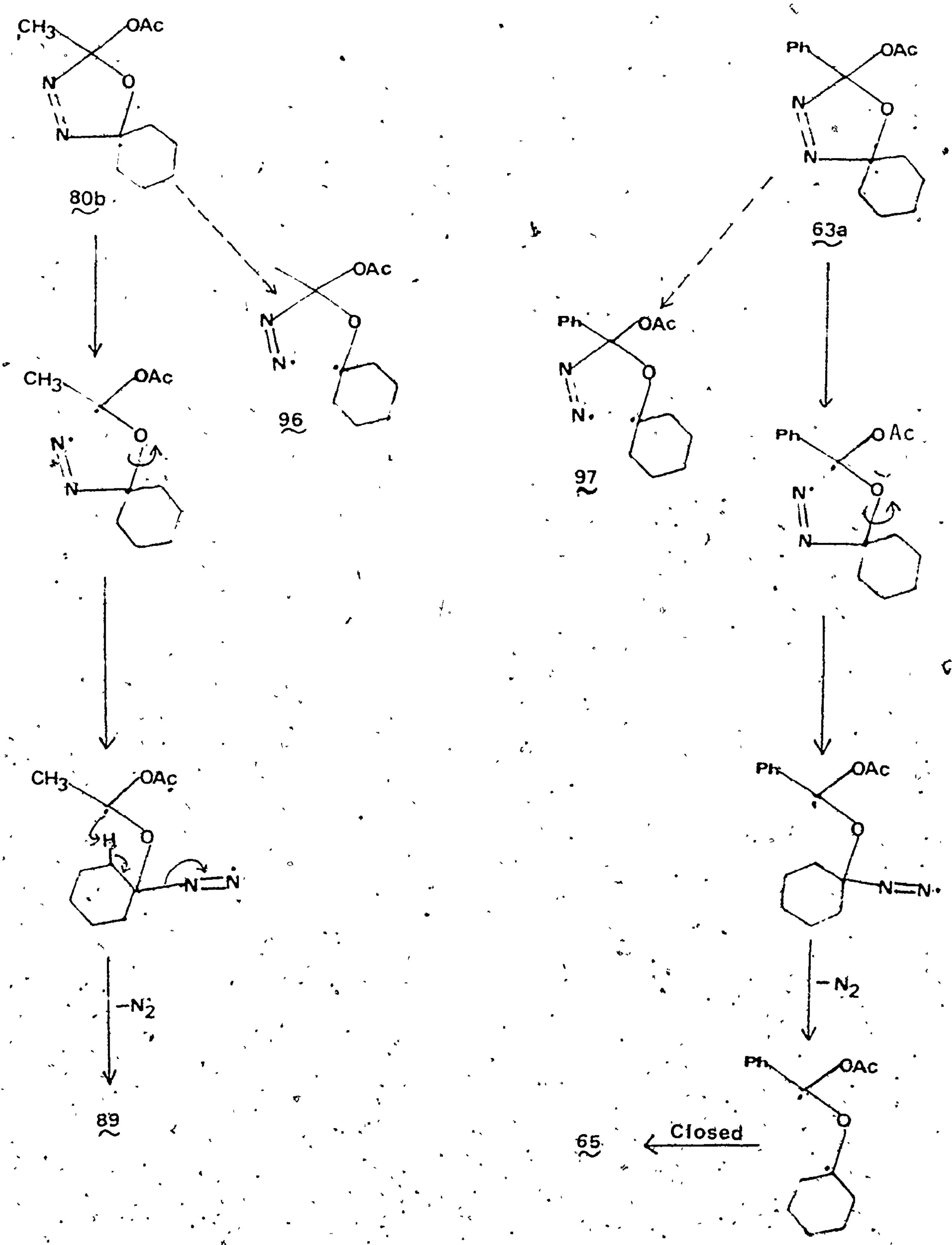
With the present data, we cannot say for sure which one of the two bonds ($N-C_2$ and $N-C_5$) breaks first. However, we observed experimentally that about 90% of enol ethers, 88 and 89, were obtained upon thermolysis of 80a and 80b, respectively. This must mean that the abstraction of hydrogen must be very fast and efficient in the course of decomposition of 80. As discussed above, the abstraction step is expected to be faster in path d than in path c. Therefore, based on this, path d is then the more likely mechanistic route for decomposition of 80.

One further piece of evidence that might support path d and against path c as the mechanism for the thermolysis of 80 is given in the following. The results of thermolysis of 80 were completely different from those reported by Hoffmann on the similar oxadiazolines 63 (equation [113]), most probably because the phenyl group in 63 can stabilize the radical centre thus making the hydrogen abstraction step very sluggish. The differences are shown in Scheme XII, using 80b and 63a as examples. If the initial cleavage of 80b and 63a leads to the diradicals 96 and 97, respectively, then we should not expect to see any great difference between our products and those reported by Hoffmann. Since the products are, in fact, unrelated, it follows that 96 and 97 are not intermediates in the thermolyses.

Photolysis (300 nm, 0°C) of 80a in chlorobenzene (which has no absorption at $\lambda = 300$ nm) in air gave the same products as those from thermolysis, and hence gave no further information about the mechanism.

Moreover, attempts to capture intermediate(s) with norbornadiene,

Scheme XII



CH3
OAc
N
N
O
80b
OAc
N
N•
O
96
Ph
OAc
N
N
O
63a
Ph
OAc
N
N•
O
97
CH3
OAc
N•
N
O
Ph
OAc
N•
N
O
CH3
OAc
H
O
N=N•
Ph
OAc
O
N=N•
−N2
89
−N2
Ph
OAc
O
65
Closed

tetracyanoethylene and phenyl isocyanate in the course of thermolysis of 80a were unsuccessful. This is the expected result if a carbonyl ylid is not an intermediate. The failure of such traps to intercept the proposed diradical intermediate is understandable, for neither radical site is expected to add rapidly to a CC or heteroatom π-system in an intermolecular reaction. Therefore, an efficient intramolecular process might well predominate.

Basic questions concerning stepwise decomposition of diazenes have to do with the energetics. Why should only one bond break (paths c or d) when there is so much driving force for breaking two (path a)? What is the driving force for breaking one N(sp^2) to C bond at a relative low temperature (80°C)? Although evidence for stepwise decomposition of azo compounds is mounting (see page 5), there is little understanding of the factors that lead to a favouring of the stepwise mechanism over the concerted alternative. Extensive radical stabilization at both sites in the present case ($\mathrm{R{-}\underset{\cdot\cdot}{\ddot{O}}{-}\underset{|}{\dot{C}}{-}OR} \longleftrightarrow \mathrm{R\underset{\cdot\cdot}{\overset{\cdot +}{O}}{-}\underset{|}{\overset{-}{C}}{-}OR}$ and $\mathrm{R{-}\ddot{N}{=}\dot{N}{:}} \longleftrightarrow \mathrm{R{-}\overset{+}{\dot{N}}{=}\overset{-}{\ddot{N}}{:}}$) may be responsible for the ease of breaking one bond without the other.

CHAPTER 6

EXPERIMENTAL

6.1 General

Proton magnetic resonance spectra were obtained with Varian T-60, Varian HA-100 or Bruker WH-90 instruments using carbon tetrachloride as the solvent (unless otherwise indicated) and TMS as internal reference. The resonances are reported in δ values (ppm), followed in brackets by the multiplicity symbol (s = singlet, d = doublet, t = triplet, q = quartet, qe = quintet, se = septet, m = multiplet), the relative proton integral and the apparent coupling constant (J), where appropriate. ^{13}C spectra were taken on a Bruker WH-90 instrument using $CDCl_3$ as solvent and TMS as internal reference.

Infrared spectra were recorded on Perkin-Elmer Models 337 and 283 instruments and on a Beckman IR-5 instrument. The spectra were taken in CCl_4 solutions (unless otherwise indicated) in 0.1 mm NaCl cells, and the data are presented in reciprocal centimeters. Spectra were calibrated with a polystyrene reference.

Ultraviolet spectra were obtained on a Cary Model 14 using quartz cells with ethanol (95%) as the solvent, and the data are given in nanometers.

Mass spectral molecular weights are based on low resolution spectra from a Hitachi RMU-6A instrument.

Electron spin resonance spectra were obtained with a JES-3BS-X, esr instrument, using Mn^{2+} marker.

Gas chromatographic analyses were done on a Varian Aerograph A90-P3.

All the melting points were determined by using a Thomas Hoover Capillary Melting Point apparatus. All values reported are uncorrected.

Refractive indices were determined with an Abbe Model 3L refractometer.

Raman spectra were taken with a Spex 1400, 3/4 Meter, Czerny Turner Spectrometer.

Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, New York (unless otherwise indicated).

The chemicals used came from Aldrich, J.T. Baker, Matheson, Fisher or BDH unless otherwise indicated. Chemicals were purified before use, wherever appropriate.

6.2 Preparation of Benzophenone Hydrazone

The compound was prepared by refluxing benzophenone (100 g, 0.55 mol) with 85% hydrazine hydrate (75 g, 1.28 mol) in absolute ethanol (100 ml) for 24 hours. The solution was cooled to room temperature and subsequently to ice temperature. Filtration of the colourless needles and recrystallization from hot 95% ethanol gave 75 g (69% yield) of hydrazone. M.p. 96-97°C (lit.[278] m.p. 97-98°).

P.m.r.: δ 6.33 (broad, 2), δ 7.13-7.57 (m,10)

I.r.: 3450, 3050, 3000, 1950, 1870, 1800, 1750, 1620, 1570, 1540, 1490, 1440, 1365, 1270, 1170, 1060, 1020, 950, 912, 700, 690, 650 cm^{-1}.

6.3 Preparation of Diphenyldiazomethane

A mixture of benzophenone hydrazone (39 g, 0.20 mol), anhydrous sodium sulphate (45 g, 0.32 mol), 600 ml ether, 15 ml ethanol saturated with potassium hydroxide and yellow mercury(II) oxide (105 g, 0.45 mol) was shaken for 75 min. at room temperature in a plastic bottle wrapped with a wet towel. The solution was filtered and the solvent was removed from the filtrate with a rotary evaporator at room temperature. The dark red oil thus obtained was dissolved in petroleum ether (b.p. 30-60°) and again filtered. Removal of the solvent from the filtrate similarly gave an oil. Freezing this oil in a stoppered flask with dry ice and then allowing the flask to warm spontaneously to room temperature gave dark crystals which then were dried on a porous plate. The product (35 g, 90% yield), m.p. 29-30° (lit.^{279} 29-32°) was then kept cold in a refrigerator, since on standing at room temperature it will decompose to yield benzophenone azine.^{280}

P.m.r.: δ 7.30 (singlet with multiplets at the bottom).

I.r.: 3020, 3010, 2100, 1570, 1490, 1450, 1445, 1360, 1350, 1275, 1185, 1075, 1030, 935, 895, 690, 650 cm^{-1}.

6.4 Preparation of Grignard Reagents

A number of Grignard reagents, (iso-propyl, ethyl, allyl, cyclohexyl and benzyl), were prepared for synthesizing the corresponding benzophenone substituted hydrazones via the reaction with diphenyldiazomethane.^{230} No attempts were made to estimate either the yield or the purity of the prepared Grignard reagents. They were used immediately. However, based on the amount of diphenyldiazomethane used in the subsequent reactions, they all were formed in roughly 85% yield. The following description is typical of all preparations.

To Grignard-quality magnesium (10.0 g, 0.42 g atom) turnings, covered with 200 mg anhydrous ether, in a 500 ml three-necked, round-bottomed flask equipped with a magnetic stirrer, a reflux condenser and a 100 ml dropping funnel, was added 2-bromopropane (32.0 ml, 0.34 mol). About 5 ml of 2-bromopropane was added all at once to start the reaction. Stirring was begun, and the remaining 2-bromopropane was added dropwise during 2.5 hours. The mixture was then refluxed for one hour before cooling down for subsequent reactions with diphenyldiazomethane.

6.5 Preparation of Benzophenone Substituted Hydrazones ($\phi_2C=NNHR$)

The compounds were either prepared by direct coupling of the corresponding substituted hydrazines with benzophenone or by the reactions of alkyl lithium or Grignard reagent with diphenyldiazomethane.[230] The three routes of preparation are described in the following paragraphs.

6.5.1 Preparation of benzophenone tert-butylhydrazone

Diphenyldiazomethane (4.0 g, 0.021 mol) was dissolved in 10 ml each of benzene and cyclohexane in a 250 ml, septum-sealed flask equipped with a stirring bar. The flask was flushed with dried nitrogen and cooled with ice before tert-butyllithium (0.024 mol, 25.0 ml of 0.97 M reagent in pentane, from Aldrich Chemicals) was added from a syringe during 15 min. The solution turned dark brown and became semisolid. The ice bath was removed and the flask was shaken occasionally during 15 min. before anhydrous ether (30 ml) was added to the mixture to dissolve the dark, oily material. Cold, saturated NH_4Cl solution was added slowly until the colour of the solution turned to yellow-orange (80-100 ml). The organic layer was separated and the aqueous layer was extracted twice with ether. Drying the combined organic extracts with anhydrous Na_2SO_4, followed by evaporation of the solvents under vacuum left a yellow-orange oil. Crystallization from aqueous ethanol gave a yellow solid, 77% yield, m.p. 74-75°C (lit.[232] m.p. 73.5-75°C).

More rapid addition of the tert-butyllithium or increasing the stirring time before work-up reduced the yield of product, sometimes drastically.

6.5.2 Preparation of benzophenone phenyl- (methyl- or 2-hydroxyethyl-) hydrazone

A mixture of benzophenone (0.30 mol), methyl- or phenylhydrazine (0.33 mol) and glacial acetic acid (30 ml) in methanol (100 ml) was refluxed under nitrogen for 1-2 hours. Colourless crystals, which appeared on cooling to ice temperature, were filtered and recrystallized from hot methanol.

Benzophenone 2-hydroxyethylhydrazone was prepared by refluxing a mixture of benzophenone (54 g, 0.296 mol), 2-hydroxyethylhydrazine (22.5 g, 0.296 mol) and acetic acid (1 ml) in benzene (120 ml) for 72 hours, with continuous removal of water formed using a Dean Stark trap apparatus. The solution was filtered through a cone of anhydrous Na_2SO_4, and the solvent was removed under vacuum with a rotary evaporator. The pale yellow solid left was recrystallized from benzene-pentane.

6.5.3 Preparation of benzophenone isopropyl- (benzyl, ethyl, cyclohexyl, or allyl)hydrazone

The synthesis was based on the reported reactions between Grignard reagents and diphenyldiazomethane.[230] The following description is typical of all preparations.

A solution of diphenyldiazomethane (45.0 g, 0.23 mol) dissolved in anhydrous ether (200 ml) was slowly added in the course of one hour to a stirred solution of freshly made isopropylmagnesium bromide (Grignard reagent), cooled by ice, prepared from isopropyl bromide (32.0 ml, 0.34 mol). Upon completion of the addition, the mixture was further stirred for 25-30 min; the red solution became nearly colourless and a yellow precipitate formed. The mixture was hydrolyzed with ammonium chloride solution and ice water, the ether layer was separated, and the water layer was extracted twice with more ether. The combined etheral layers were dried over Na_2SO_4 and then evaporated under vacuum with a rotary evaporator. A yellow sticky liquid was obtained in about 90% yield.

The yields and properties of the hydrazones prepared are listed in Table 1 (page 66).

6.6 Preparation of Lead Tetraacetate (LTA)

The method used was similar to that of Fieser.[281] A mixture of acetic acid (600 ml) and acetic anhydride in a 3-litre, three-necked, round-bottomed flask was heated to 55-80°C. While the mixture was stirred vigorously with a mechanical stirrer, lead tetraoxide (red lead oxide) (700 g, 1.03 mol) was added in portions of 15-20 g. A fresh addition was made only after the colour due to the preceeding portion had largely disappeared. The temperature was kept between 55° and 80° at all times. At the end of the reaction, the thick and somewhat dark solution was cooled, and the crude product was filtered, washed with cold acetic acid and then recrystallized from hot acetic acid. The yield was 65% (300 g).

6.7 Preparation of Alkylazodiphenylmethylacetates ($\phi_2\underset{\text{OAc}}{\text{C}}\text{N=NR}$)

6.7.1 By oxidation with lead tetraacetate (LTA)

The procedure used was similar to that of Iffland.[184] The following description is typical.

A solution of benzophenone phenylhydrazone (13.6 g, 0.05 mol) dissolved in methylene chloride (50 ml) was added in the course of 20 minutes to a stirred solution, at 0°C under nitrogen, of lead tetraacetate (25 g, 0.055 mol) dissolved in methylene chloride (150 ml). Stirring was continued for another 20 minutes before cold water (150 ml) was added. A heavy brown sludge which formed was removed by filtering the entire mixture through a bed of Celite. The methylene chloride layer was separated and washed successively with water and dilute sodium bicarbonate solution (5%) until free of acetic acid. After drying over anhydrous Na_2SO_4, the solvent was removed under vacuum with a rotary evaporator, and the pale yellow solid which remained was recrystallized from methanol to give 13.5 g (82%) of pure product.

6.7.2 Oxidation with bromine

A solution of benzophenone tert-butylhydrazone (2.0 g, 8.0×10^{-3} mol) in glacial acetic acid (100 ml) containing sodium acetate trihydrate (10.0 g) was stirred and cooled with ice while bromine (1.40 g, 4.4×10^{-3}

mol) in glacial acetic acid (20 ml) was added in the course of 10-15 min. Ice water (200 ml) was added and the resulting mixture was extracted with methylene chloride until the aqueous layer was colourless. The combined methylene chloride extract was washed, first with water and then with 5% sodium bicarbonate solution, to remove acetic acid. Drying over anhydrous Na_2SO_4, followed by evaporation of solvent with a rotary evaporator, left 1.90 g (77%) of crude product as a yellow oil containing some benzophenone (ν_{CO} 1650 cm^{-1}). The oil was dissolved in pentane from which crystals separated after 5 days in a refrigerator. The yield of t-butylazodiphenylmethyl acetate was 35%.

The azoacetates which were prepared are gathered in Table 2 (page 71) together with yields, m.p., pmr, ir and analyses.

6.8 Preparation of α-Azodiphenylcarbinols, $\phi_2\underset{OH}{C}N=NR$

Generally, 0.05 mole of each azoacetate was treated with 0.12 mole of methyllithium in ether in a common procedure with the only variation being the amount of solvent needed or co-solvents used to attain solution of the reagents. The following description is typical.

A solution of tert-butylazodiphenylmethyl acetate (15.5 g, 0.05 mol) in 200 ml of anhydrous ether, under nitrogen, was cooled to -10°C. Methyllithium (0.13 mol, 75 ml of 1.7 M reagent in ether) was added by drops from a syringe, with stirring, during 10 min. After 15 min more, ice-cold, saturated NH_4Cl solution (250 ml) was added slowly. After separation of the organic layer, the aqueous phase was extracted thrice with ether. The ethereal fractions were combined, dried with anhydrous Na_2SO_4, and concentrated (without heating) under reduced pressure with a rotary evaporator. The pale yellow residue which remained was recrystallized from n-pentane.

The yields of the products were of the order of 70-75%. The α-azodiphenylcarbinols which were synthesized are listed in Table 3 (page 73) together with their properties.

6.9 Chemistry of α-Azodiphenylcarbinols

6.9.1 Thermolysis

The compounds were dissolved in carbon tetrachloride and heated at 35°C. Bubbling started immediately and subsided within a few hours. The major products from the decomposition were the corresponding chlorides RCl, chloroform and benzophenone. The chlorides RCl and chloroform were identified by pmr and by comparing their retention times on several glpc columns with those of authentic samples.

Evaporation of the volatile products at the vacuum pump, addition of a small amount of methanol to the residue and treatment of the resulting mixture with 2,4-dinitrophenylhydrazine reagent gave benzophenone 2,4-dinitrophenylhydrazone, m.p. 238°C (lit.[282] m.p. 238°C).

Decomposition of several α-azocarbinols under similar conditions in benzene gave the corresponding compounds RH and benzophenone as the major products.

6.9.2 Kinetics of decomposition of tert-butylazodiphenylcarbinol (76)

Experiments were carried out in nmr tubes at the temperature of the Varian-T60 probe (35°C). Slow runs were also done with a constant temperature water bath (35° ± 0.1°C) from which tubes were transferred at 1 hour intervals to the probe for integration. For kinetic runs with oxygen present, the tubes were capped while they were in the probe, but they were removed at regular intervals for shaking and for venting of accumulated gas. Kinetic runs with oxygen absent were performed using sealed nmr tubes. Solutions in the tubes were put through three or more freeze-pump-thaw cycles (vacuum line pressure < 0.01 torr) before sealing.

About 20 integrals of the tert-butyl signals of tert-butylazodiphenylcarbinol (δ 1.33) and of tert-butyl chloride (δ 1.60) were recorded for runs in CCl_4, the time intervals between integrals ranging from 1 min to 1 hour, depending on whether or not air was excluded.

Standard first-order treatment of the data gave straight, least-squares fits to the equation $\ell n \frac{a}{a-x} = kt + C$, with small positive values of C except in the case of concentrated solutions in benzene.

The major products from decomposition of tert-butylazodiphenylcarbinol in CCl_4 were tert-butyl chloride, chloroform and benzophenone. Isobutane could not be detected by pmr or glpc. Tert-butyl chloride and chloroform were identified by pmr and by comparing their retention times on several glpc columns with those of authentic samples. The yields of tert-butyl chloride (89%) and chloroform (96%) were estimated by glpc after addition of a weighed quantity of chlorobenzene, which served as a standard. A 10 ft x 0.25 in. column packed with Carbowax 20 M (15%) on 60-80 mesh Chromosorb A was used at 110°C with a helium flow rate of 120 ml/min. Peak areas were estimated by cutting and weighing.

Evaporation of the volatile products at the vacuum pump, addition of a small amount of methanol to the residue, and treatment of the resulting mixture with 2,4-dinitrophenylhydrazine reagent gave benzophenone

2,4-dinitrophenylhydrazine, m.p. 238° (lit[282] m.p. 238°C).

Isobutane, from decomposition of tert-butylazodiphenylcarbinol in benzene and in carbon tetrachloride with added thiophenol, was detected in the pmr spectrum as a doublet (J = 6.0 Hz) at δ 0.89. The identity of the product producing that signal was confirmed, both by glpc and by pmr, with solutions prepared by bubbling isobutane (Matheson) into carbon tetrachloride (or benzene).

Yields of isobutane were estimated by calculating that fraction of the total high field integral which was contributed by the isobutane doublet. Reactions in degassed benzene gave isobutane yields near 91%. In CCl_4 with thiophenol (0.02 M) added, the yield of isobutane was 60% and the yield of tert-butyl chloride was 40%.

Isobutene from decomposition of tert-butylazodiphenylcarbinol in degassed benzene was detected as described below. Spent solutions from several kinetic runs were cooled before the nmr tubes were cut and the contents were transferred to a bulb attached to a vacuum line. The bulb was cooled with liquid N_2 during evacuation and was allowed to warm while another receiver on the line was cooled to receive volatile material from the bulb. Distillate thus collected was then allowed to volatilize into the vacuum line. A sample of the gas was analysed by ms with a Hitachi RMU6A instrument using 9 eV electrons. The ratio of peaks corresponding to isobutane and isobutene (mass 58:mass 56) was 100:2. A sample of isobutane (Matheson) gave a negligible signal for mass 56, relative to that for mass 58, at the same instrument settings.

Some of the gas remaining in the vacuum line was condensed into the N_2-cooled gas sampling loop of the gas sampling accessory for the Varian Aerograph A90-P3 gas chromatograph. Simultaneous switching to the injection mode and heating of the loop with hot water injected the sample onto the 10 ft x 0.25 in. column packed with SE 550 (31.) on firebrick. The same column had been used previously to separate isobutane from the isomeric butenes.[283] Instrumental conditions similar to those described[283] led to two signals the areas of which were estimated by triangulation. The ratio of isobutane to isobutene found was 100:0.9. Injection of a mixture of isobutane and isobutene prepared from authentic samples (Matheson) was carried out to confirm identities.

Attempts to detect diphenylcarbinol in the benzophenone fraction by either ir or tlc were not successful. An authentic mixture of diphenylcarbinol and benzophenone could be separated by tlc on silica gel plate using chloroform as the eluting solvent. When experiments were carried out on the sample from the benzophenone fraction, under the same conditions, no spots corresponding to diphenylcarbinol on the tlc plates were observed.

The rate constants of the decompositions are assembled in Table 4 (page 79).

6.9.3 Effects of thiophenol, phenol and triphenylstannane on the decomposition

The effect of the titled reagents on the decomposition of t-butylazodiphenylcarbinol was examined. To a solution of t-butylazodiphenylcarbinol in benzene or carbon tetrachloride was added a small amount of thiophenol or phenol. An immediate substantial increase in the rate of bubbling rate did not increase so much compared with thiophenol or phenol.

6.9.4 Spin trapping by nitrosobenzene

A benzene solution of an α-azocarbinol and nitrosobenzene in an open tube at room temperature gave a strong, "triplet-natured" esr signal. A degassed sample gave a more complex spectrum in which each of the three "humps" was split into more lines. Mn^{2+} was used as a marker in the spectra in all cases. A portion of the nitrosobenzene solution without added α-azodiphenylcarbinols did not produce an esr signal at the same instrumental settings. The a_N and g values of the nitroxides formed are assembled in Table 10 (page 111).

6.9.5 Trapping with unsaturated compounds

In a typical procedure, the unsaturated substrate (c.a. 0.008 mol) was added to a solution of α-azocarbinols (0.002 mol) in benzene (4.0 ml). The mixture was stirred or shaken until it was homogeneous before it was heated at 35-52°C for 12-20 hours in a septum-stoppered flask vented with a syringe needle. Vigorous gas evolution was observed in all cases either immediately after mixing or soon after heating had started. In most cases, the bubbling stopped well before the end of the heating period. Bulb-to-bulb distillation under vacuum left behind the benzophenone and telomeric material, if any. Analytically pure products were obtained by glpc. A 10 ft x 0.25 in. column packed with Carbowax 20 M (15%) on 60-80 mesh Chromosorb A was used at 80-120°C with a helium flow rate of 45-60 ml/min.

Yields of all the products (except with azobenzene) were estimated by glpc after addition of tert-butylbenzene in known quantity to the distillate. The thermal conductivities of tert-butylbenzene and of acrylonitrile, determined by injecting a mixture of known composition were found to be the same within experimental error. Tert-butylbenzene was used as the standard for all products without correction for differences in thermal conductivities, if any.

For reactions of azobenzene with α-azocarbinols (t-butyl, isopropyl, ethyl and methyl), the yields were estimated by pmr after addition of tert-butyl bromide to a portion of the crude reaction mixtures. In other cases, the yields reported were the isolated yields. Isolation of the substituted 1,2-diphenylhydrazine adducts was done either by column chromatography on basic alumina (80-200 mesh, Brockmann, activity grade 1) or by thin layer chromatography on Al_2O_3 plates (from Brinkman Instruments, Inc.) with petroleum ether-benzene or chloroform as eluting solvents. The products were then recrystallized either from benzene-^{n}pentane, methanol, or methanol-water.

Results of reactions of α-azodiphenylcarbinols with olefinic substrates and with azobenzene are gathered in Tables 5-9 (pages 85-89).

6.9.6 Reactions of methylazodiphenylcarbinol with norbornene in the presence of D_2O

To a solution of methylazodiphenylcarbinol (1.0 g, 4.4 mmol) in benzene (10 ml), in a reaction vessel fitted with top-driven magnetic stirrer,[284] was added D_2O (5 ml). The mixture was stirred at room temperature for 5-10 min before norbornene (1.6 g, 17.0 mmol) was added all at once. The resulting mixture was heated at 35°C, with continuous vigorous stirring, for 36 hours. Analytically pure sample was obtained by glpc. The yield (50%) was estimated by glpc using the internal standard method. More than 87 atom of D (from m.s.) was found to be incorporated into the adduct.

6.9.7 Reactions of olefins in the presence of phenol

Acrylonitrile and crotonaldehyde were the two olefins used for this study. The procedure for the reactions was similar to that in section 6.9.5. The yields of the adducts, 4-methylacrylonitrile and 3,4-dimethylpentanal, were estimated by glpc after addition of a weighed quantity of chlorobenzene or tert-butylbenzene, which served as an internal standard. A 10 ft x 0.25 in. column packed with Carbowax 20 M (15%) on 60-80 mesh Chromosorb A was used at 130°C with a helium flow rate of 45 ml min^{-1}. Peak areas were estimated by triangulation. The results are tabulated in Tables 18-29 below.

Table 18: Effect of Initial Concentration of 73 (R = isopropyl) on the Yield

Crotonaldehyde: 1.318 M Phenol: 0.654 M	
Isopropylazodiphenylcarbinol, M	% Yield, ± 2%
0.041	39.5
0.164	39.2
0.327	39.0
0.491	38.5
0.654	35.0
0.818	28.0

Table 19: Effect of Initial Concentration of 73 (R = isopropyl) on the Yield

<table>
<tr><td colspan="2">Acrylonitrile: 1.354 M
Phenol: 0.668 M</td></tr>
<tr><th>Isopropylazodiphenylcarbinol, M</th><th>Yield, ± 2</th></tr>
<tr><td>0.042</td><td>70</td></tr>
<tr><td>0.167</td><td>85</td></tr>
<tr><td>0.334</td><td>86</td></tr>
<tr><td>0.501</td><td>84</td></tr>
<tr><td>0.668</td><td>86</td></tr>
<tr><td>0.845</td><td>80</td></tr>
</table>

Table 20: Effect of Concentration of Phenol

<table>
<tr><td colspan="2">Isopropylazodiphenylcarbinol: 0.348 M
Crotonaldehyde: 0.348 M</td></tr>
<tr><th>Phenol, M</th><th>% Yield, ± 2%</th></tr>
<tr><td>0.000</td><td>10.0</td></tr>
<tr><td>0.369</td><td>23.0</td></tr>
<tr><td>0.712</td><td>25.5</td></tr>
<tr><td>1.032</td><td>27.0</td></tr>
<tr><td>1.332</td><td>27.0</td></tr>
<tr><td>1.613</td><td>25.0</td></tr>
<tr><td>2.125</td><td>23.5</td></tr>
<tr><td>2.359</td><td>24.0</td></tr>
<tr><td>3.687</td><td>20.0</td></tr>
<tr><td>4.964</td><td>17.5</td></tr>
</table>

Table 21: Effect of Concentration of Phenol

<table>
<tr><th colspan="2">Isopropylazodiphenylcarbinol: 0.348 M
Crotonaldehyde: 1.394 M</th></tr>
<tr><th>Phenol, M</th><th>% Yield, ± 2%</th></tr>
<tr><td>0.000</td><td>26.5</td></tr>
<tr><td>0.336</td><td>31.0</td></tr>
<tr><td>0.648</td><td>35.5</td></tr>
<tr><td>0.940</td><td>39.5</td></tr>
<tr><td>1.469</td><td>41.0</td></tr>
<tr><td>1.711</td><td>39.5</td></tr>
<tr><td>1.937</td><td>38.0</td></tr>
<tr><td>2.543</td><td>34.0</td></tr>
<tr><td>3.360</td><td>29.5</td></tr>
<tr><td>4.004</td><td>24.0</td></tr>
<tr><td>4.524</td><td>22.0</td></tr>
</table>

Table 22: Effect of Concentration of Phenol

<table>
<tr><th colspan="2">Isopropylazodiphenylcarbinol: 0.348 M
Crotonaldehyde: 3.484 M</th></tr>
<tr><th>Phenol, M</th><th>% Yield, ± 2%</th></tr>
<tr><td>0.000</td><td>25.0</td></tr>
<tr><td>0.522</td><td>30.0</td></tr>
<tr><td>0.977</td><td>36.0</td></tr>
<tr><td>1.377</td><td>33.0</td></tr>
<tr><td>1.731</td><td>33.0</td></tr>
<tr><td>2.047</td><td>32.0</td></tr>
<tr><td>3.224</td><td>28.0</td></tr>
<tr><td>3.987</td><td>26.5</td></tr>
<tr><td>4.524</td><td>23.0</td></tr>
</table>

Table 23: Effect of Concentration of Phenol

Isopropylazodiphenylcarbinol: 0.348 M Crotonaldehyde: 1.978 M	
Phenol, M	% Yield, ± 2%
0.000	29.0
0.613	37.5
0.889	40.0
1.127	47.5
1.617	47.0
2.033	45.5
3.177	40.5
3.786	39.0
4.277	36.0

Table 24: Effect of Concentration of Phenol

Isopropylazodiphenylcarbinol: 0.348 M

Crotonaldehyde: 6.968 M

Phenol, M	% Yield, ± 2%
0.000	21.5
0.312	25.0
0.822	24.0
1.033	23.0
1.221	22.0
1.923	22.0
2.379	21.0
2.698	20.0

Table 25: Effect of Concentration of Phenol

Isopropylazodiphenylcarbinol: 0.348 M

Acrylonitrile: 0.348 M

Phenol, M	% Yield, ± 2%
0.000	45.0
0.370	63.0
0.716	64.0
1.040	61.0
1.340	60.0
1.623	60.0
1.890	58.0
2.138	55.0
2.587	55.0
2.807	52.5
3.710	50.0
4.420	45.0
4.995	42.5

Table 26: Effect of Concentration of Phenol

Isopropylazodiphenylcarbinol: 0.348 M

Acrylonitrile: 1.394 M

Phenol, M	% Yield, ± 2%
0.000	36.5
0.666	73.5
0.965	76.5
1.508	84.5
1.995	85.0
2.207	82.5
2.610	80.0
4.110	67.5
5.083	60.0

Table 27: Effect of Concentration of Phenol

Isopropylazodiphenylcarbinol: 0.348 M

Acrylonitrile: 1.978 M

Phenol, M	% Yield, ± 2%
0.000	25.0
0.637	89.0
0.925	90.0
1.445	92.5
2.114	88.5
2.580	83.0
3.936	64.0
4.868	55.0
5.523	50.0

Table 28: Effect of Concentration of Phenol

Isopropylazodiphenylcarbinol: 0.348 M Acrylonitrile: 3.434 M	
Phenol, M	% Yield, ± 2%
0.000	10.0
0.565	30.0
1.057	37.0
1.490	40.0
1.873	37.5
2.215	35.0
3.488	30.0
4.314	25.0
4.894	22.5

Table 29: Effect of Concentration of Phenol

Isopropylazodiphenylcarbinol: 0.348 M Acrylonitrile: 6.948 M	
Phenol, M	% Yield, ± 2%
0.000	1.5
0.398	16.5
0.746	22.0
1.050	25.0
1.320	26.0
1.560	29.5
2.457	30.0
3.040	24.5
3.450	17.5

6.10 Independent Syntheses of Tert-butyl-1,2-diphenylhydrazine and Methyl-1,2-diphenylhydrazine

The approach was based on the reported reaction[285] between phenyllithium and azobenzene.

A solution of azobenzene (0.03 mol) in dry benzene (100 ml) was stirred and cooled with ice during addition of alkyllithium (0.036 mol) in pentane or in ether over 10 min. After 10 min. more in the ice bath, cold, saturated, aqueous NH_4Cl was added. Separation of the benzene layer, extraction of the water layer with ether, drying of the combined organic layers and evaporation of the solvents in a rotary evaporator left a residue. Isolation of the desired hydrazine was done either by column chromatography on basic alumina (80-200 mesh, Brockmann, activity grade 1) or with alumina TLC plates (from Brinkmann Instruments, Inc.) with petroleum ether-benzene as eluting solvent. The pure products were obtained after recrystallization from methanol. The yields were of the order of 10-15%.

The spectral data (pmr, ir as well as m.s.) matched those of the product from the reactions of azobenzene with the corresponding α-azodiphenylcarbinols (Table 9).

6.11 Thermolysis of Tert-butylazodiphenylmethyl Acetate

Kinetic runs were done in nmr tubes at the constant temperature of a water bath (35.0 ± 0.1°C). Solutions of tert-butylazodiphenylmethyl acetate were prepared in benzene. The pmr spectrum was recorded and integrated before tubes were placed in the bath, from which they were removed at 10 hour intervals for integration (Varian-T60 NMR instrument).

Reaction was stopped by cooling the tubes quickly in ice water and time outside the bath was not counted.

About 12 integrals of the tert-butyl signals of tert-butylazodiphenylmethyl acetal were recorded, and standard first-order treatment of the data gave straight, least-squares fits to the equation $\ln \frac{a}{a-x} = kt + C$ with small values of C. The results are shown in Table 30.

No attempts were made to analyse the products. However, from tlc, there were at least four products formed.

Table 30: Kinetics of Decomposition of Tert-butylazodiphenylmethyl Acetate at 35°C, in Air

Solvent	Initial Concentration, M	$k \times 10^6$ sec^{-1}	Correlation Coefficient
Benzene	0.243	1.20 ± 0.04	0.996

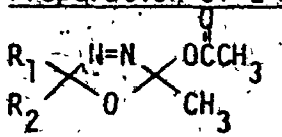
6.12 Preparation of Ketone Acetylhydrazones ($R_1R_2C{=}NNHCOCH_3$)

A mixture of ketone (0.50 mol), acetylhydrazine (0.48 mol), acetic acid (2 drops) and benzene (250 ml) was refluxed for two days, using a Dean Stark trap to remove water continuously. The resulting mixture was filtered through a cone of anhydrous Na_2SO_4. The solvent was removed under vacuum with a rotary evaporator. The white solid remaining was recrystallized from acetone or benzene-pentane mixture. The results of the two acetylhydrazones which were prepared are gathered in Table 12 (page 122) together with the yield, m.p., spectroscopic data as well as analyses.

6.13 Preparation of Acetone-d_6 Acetylhydrazone

A solution of acetylhydrazine (15.5 g, 0.21 mol) in benzene (80 ml) was refluxed for 2 hours, using a Dean Stark trap to remove water from the hygroscopic hydrazine. Deuterium oxide (5 ml) and p-toluenesulphonic acid (about 0.1 g) were added after cooling to room temperature. The resulting mixture was refluxed for 90 min, using a Dean Stark trap to remove water continuously. Another portion of D_2O (5 ml) was added, and refluxed for another 90 min. After cooling to room temperature, acetone-d_6 (15.0 g, 0.23 mol) was added. The resulting mixture was refluxed for 3 hours, still using a Dean Stark trap to remove any water formed. The solvent, after filtering through a cone of anhydrous Na_2SO_4, was removed under vacuum with a rotary evaporator. The white solid left was recrystallized from benzene-pentane mixture. The yield (23.0 g) obtained was about 92%. More than 96 atom % of D was incorporated into the hydrazone (estimated by mass spectrometry[258] and pmr analysis[268]).

6.14 Preparation of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines



A solution of acetylhydrazone (0.10 mol) dissolved in methylene chloride (80 ml) was added in the course of 20 min., under nitrogen, to a stirred solution of lead tetraacetate (0.11 mol) in methylene chloride (150 ml) at 0°C. The reaction mixture was further stirred at 0°C for 20 min. after the complete addition of acetylhydrazone. About 200 ml of water was added, and the heavy brown sludge was removed by filtering the entire mixture through a bed of Celite. The organic layer was separated and was washed successively with water and dilute sodium bicarbonate solution (5%) until free of acetic acid. After drying over anhydrous Na_2SO_4, the solvent was removed under vacuum with a rotary evaporator. The residue was vacuum distilled, bulb-to-bulb, at about 45-50°C, to produce pure product. For cyclohexanone-N-acetylhydrazone, the product crystallized from the neat in the refrigerator after 4 days. The yields were of the order of 70-80%.

Two cyclic α-azoacetates (i.e., oxadiazolines) which were prepared are shown in Table 13 together with their properties and analyses.

6.15 Preparation of 2-Acetoxy-2-methyl-5,5-bis(trideuteromethyl)-Δ^3-1,3,4-oxadiazoline

The procedure was exactly the same as that described in the previous section, 6.14. Five grams (67%) of pure product was obtained, starting from 5.0 g of acetone-d_6 acetylhydrazone. It was estimated both by mass spectrometry (using the peak m/e = [M-28]) and pmr analysis that the deuterium content was better than 96 atom %.

6.16 Chemistry of 2-Acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines

6.16.1 Thermolysis

The Δ^3-1,3,4-oxadiazoline (0.02 mol) in a solution prepared from 15 ml benzene was heated at the reflux temperature for 2 days. Yields were determined by glpc of the crude, after addition of t-butylbenzene as internal standard, were separated by glpc (10' x 0.25", 20% SE-30, 75-155°, 45 ml min^{-1}) after distillation of 13 ml of benzene from the solution.

Pyrolysis in carbon tetrachloride, chlorobenzene, or nitrobenzene in NMR tubes, under similar conditions, gave the same results.

The results are listed in Tables 15 and 16 (page 130-131), together with the spectroscopic data and analyses.

6.16.2 Kinetics of thermolysis of 2-acetoxy-2-methyl-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline and 2-acetoxy-2-methyl-5,5-bis(trideuteromethyl)-Δ^3-1,3,4-oxadiazoline

Solutions of 2-acetoxy-2-methyl-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline and its deuteriated analog in benzene and/or in nitrobenzene (Table 17, page 134) containing anisole were prepared free of air with several freeze-pump-thaw cycles before they were sealed in NMR tubes. The concentration of anisole was about 1/3 that of the compound under study. The pmr spectrum was recorded before tubes were placed in a bath at 79.0° ± 0.1°C, from which they were removed at 2-3 hour intervals for analysis. Reaction was stopped by cooling the tubes quickly in cold water and time outside the bath was not counted. Peak heights of pmr signals were normalized with respect to the internal standard (i.e., anisole). The reactions were followed to 85% of completion. Standard first-order treatment of the data gave straight, least-squares fits to the equation $\ln \frac{a}{a-x} = kt + C$ with small value of C.

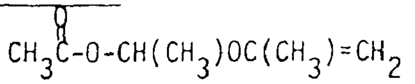
The products in the two cases were the same except for the labelling with deuterium. The kinetic results are assembled in Table 17 (page 134).

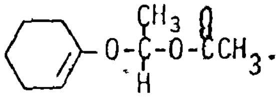
6.16.3 Attempts to trap intermediates in pyrolysis of 2-acetoxy-2-methyl-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline with phenylisocyanate

To Δ^3-1,3,4-oxadiazoline (1.0 g, 5.8 mmol) was added a solution of phenylisocyanate (1.9 g, 16 mmol) in 5 ml benzene (or 10 ml neat phenylisocyanate). The resulting mixture was then heated under the same conditions as in the pyrolysis experiments described previously. No intermediates were trapped, and the pyrolysis products were the same as before.

Attempts to use norbornadiene, or tetracyanoethylene as trapping agent under similar conditions were also unsuccessful.

6.17 Reactions of 1-Acetoxyethyl-2-propenyl Ether ($CH_3CO_2CH(CH_3)OC(CH_3)=CH_2$) 88 with Bromine

To  $CH_3\overset{O}{\overset{\|}{C}}\text{-O-}CH(CH_3)OC(CH_3)=CH_2$ (0.05 g, 0.35 mmol) in CCl_4 (0.5 ml) was added bromine solution (0.3 g in 0.5 ml CCl_4) by drops at room temperature until there was a pale yellow colour persistent. The reaction was followed by pmr. A rapid decolourization of bromine was observed and the corresponding dibromide, along with some minor products, was formed (from pmr). The dibromide pmr spectrum was: δ 1.97 (d,3,J=6.0 Hz), δ 2.07 (s,3), δ 2.33 (s,3), δ 3.76 (s,2), δ 6.69 (q,1,J=6 Hz). Shaking the solution with water (2 drops) at room temperature for one hour gave acetaldehyde, acetic acid and bromoacetone (proof from pmr).

Under the same conditions, a rapid decolourization of bromine was also observed when bromine reacted with . However, there was no corresponding dibromide observed. No attempts to identify the products in this case were made.

6.18 Preparation of 2-Acetoxy-3-methylbut-2-ene

A solution of 3-methylbutan-2-one (50 g, 0.58 mol), acetic anhydride (90 g, 0.88 mol) and p-toluenesulphonic acid (1 g) was refluxed for 20 hours. Methanol (40 ml) was then added at 0°C into the resulting mixture and stirred overnight. Water (200 ml) was then poured in and solid $NaHCO_3$ was added in small portions at 0°C until neutralization. Separation of the organic layer, extraction of the water layer with ether, drying of the combined organic layers over Na_2SO_4 and distillation gave 23% (17.0 g) of pure product. Its properties are listed below.

B.p.: 124-127°C (lit[286] 124-126°C)

Refractive index: $n_D^{26} = 1.4195$ (lit[286] 1.4114)

P.m.r.: The broad singlets at δ 1.52, 1.70 and 1.80, totalling 9 hydrogens were assigned to three $C=C-CH_3$ methyl groups. A singlet at δ 2.03 of 3 hydrogens was assigned to the acetoxy methyl group. The pmr spectrum reported in the literature[287] is in good agreement with that reported above.

I.r.: 3000, 2920, 2870, 1760, 1705, 1445, 1395, 1378, 1370, 1215, 1140, 1015, 935, 860 cm^{-1}.

Mol. wt. calcd. for $C_7H_{12}O_2$: 128; found (m.s.): 128.

6.19 Preparation of 2-Acetoxy-2,3-epoxy-3-methylbutane

To a dry solution of m-chloroperbenzoic acid (5.0 g, 0.029 mol) in chloroform (60 ml) at 0°C standing over Na_2SO_4 (10 g) was added, in one portion, 2-acetoxy-3-methylbut-2-ene (4.0 g, 0.031 mol). The solution was stirred at 0°C for 9.5 hours, at which time most of the m-chloroperbenzoic acid had been used. The Na_2SO_4 was removed by filtration and the solution was washed twice with 20% K_2CO_3 solution, twice with water and dried over Na_2SO_4. The solvent chloroform was removed at room temperature under vacuum with a rotary evaporator. About 60% (2.5 g) of pure product was then obtained by vacuum distillation (~ 0.05 mm Hg) at about 30-40°C. The compound was stable at room temperature for at least three weeks. Its properties are listed below.

P.m.r.: δ 1.25 (s,3), δ 1.32 (s,3), δ 1.59 (s,3), δ 2.02 (s,3).

I.r.: 2000, 2980, 2940, 1750, 1730, 1705, 1490, 1450, 1380, 1375, 1247, 1238, 1180, 1145, 1125, 1018, 935, 900, 883, 680, 665, 625 cm^{-1}.

Mol. wt. calcd. for $C_7H_{12}O_3$: 144, found (m.s.): 144.

Anal. calcd. for $C_7H_{12}O_3$: C 58.32, H 8.39; found: C 58.59, H 8.51.

6.20 Thermolysis of 2-Acetoxy-2,3-epoxy-3-methylbutane in Benzene and in Carbon Tetrachloride Solutions

3-Acetoxy-2,3-epoxy-3-methylbutane (0.5 g, 3.5 mmol) in a solution prepared from benzene (2.0 ml) was heated at the reflux temperature for two days. Similar conditions were used to carry out the thermolysis in carbon tetrachloride. The thermolysis gave nearly quantitatively the rearrangement product, 3-acetoxy-3-methylbutan-2-one; its spectroscopic data (pmr and ir) are listed below.

P.m.r.: δ 1.40 (s,6), δ 2.03 (s,6).

The pmr spectrum reported in the literature[288] is in good agreement with that reported here.

I.r.: 2990, 2940, 1748, 1734, 1708, 1407, 1440, 1385, 1375, 1358, 1250, 1160, 1125, 1020, 965 cm^{-1}.

CHAPTER 7

SUMMARY

In the present thesis, a series of acyclic α-azodiphenylcarbinols **73** were synthesized and their chemistry was investigated. The synthesis of **73** consists of five steps with overall yield of about 20 .

Several pieces of evidence have established that **73** undergo concerted, radical-chain, induced decomposition by attack at the hydroxyl hydrogen. These include kinetic measurements, spin trapping with nitrosobenzene, as well as hydroalkylation of unsaturated compounds. The failure of several common inhibitors (e.g., phenol, thiophenol, triphenylstannane) to stop the chain decomposition is attributed to a concerted mechanism, which brings the combined heats of formation of nitrogen and of a carbonyl group (i.e., CO in benzophenone) into play, to lower the free energy of activation. Azo compounds are not normally susceptible to induced decomposition; the present unusual triggered decomposition of **73** provides a new mechanistic pathway for decomposition of azo compounds.

The synthetic utility of **73** was found to be high. Various new compounds can be synthesized via radical chain addition of RH (from **73**) to the unsaturated compounds. The thermochemistry for such addition is always favourable by virtue of the heats of formation of nitrogen and of benzophenone. Azobenzene has been found to be a good substrate to capture the radicals R· from **73**, and this therefore provides a new synthetic route for synthesis of 1,2-diphenyl-1-substituted hydrazines. The successful addition of ethanol (via 73 with R = CH_2CH_2OH) across the azo linkage of azobenzene, yielding 1,2-diphenyl-1-β-hydroxyethyl hydrazine, provides a unique example of addition of a primary alcohol to give a primary alcohol product and demonstrates that β-hydroxyethyl radicals can be generated conveniently by the azocarbinol route.

The discovery of phenol as a catalyst in radical chain reactions is significant, since catalysis in chain reactions is currently rare. Optimum phenol and olefin concentrations, leading to maximum yields of the adducts, were estimated.

The reaction of LTA with ketone acetylhydrazones has been investigated. In methylene chloride solution, oxidative cyclization occurred readily to give 2-acetoxy-2-methyl-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines. The structures of these new compounds were established from the spectroscopic data, chemical reactivities, products from thermolysis, as well as analyses. The mechanism proposed for the decomposition of these compounds involves stepwise opening of the five-membered ring to form a diradical intermediate, with concerted hydrogen abstraction and nitrogen elimination following a rotation about the O-C bond of the diradical intermediate.

REFERENCES

1. Comprehensive treatments of free-radical chemistry will be found in: (a) C. Walling, Free Radicals in Solution, Wiley, N.Y., 1957; (b) E.S. Huyser, Free-Radical Chain Reactions, Wiley-Interscience, N.Y., 1970; (c) J.K. Kochi, Ed., Free Radicals, Vols. I and II, Wiley, N.Y., 1973; (d) W.A. Pryor, Free Radicals, McGraw Hill, N.Y., 1966; (e) R.L. Huang, S.H. Goh and S.H. Ong, The Chemistry of Free Radical, Edward Arnold, Ltd., London, 1974; (f) D.C. Nonhebel and J.C. Walton, Free Radical Chemistry, Cambridge University Press, Cambridge, 1974.
2. M. Gomberg, Ber. 33, 3150 (1900), and J. Amer. Chem. Soc., 22, 757 (1900).
3. H. Wieland, Ann. Chim., 381, 200 (1911).
4. F. Paneth and W. Hofeditz, Ber. 62B, 1335 (1929).
5. F. O. Rice and K.K. Rice, The Aliphatic Free Radicals, The John Hopkins Press, Baltimore, 1935.
6. D.H. Hey and W.A. Waters, Chem. Rev., [illegible]1, 202 (1937).
7. M.S. Kharasch, H. Engelmann and F.R. Mayo, J. Org. Chem., 2, 288 (1937).
8. P.J. Flory, J. Amer. Chem. Soc., 59, 241 (1937).
9. For a review, see T. Koenig, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York, 1973, p. 113.
10. S.W. Benson, J. Chem. Phys., 40, 1007 (1964).
11. (a) R. Hiatt, J. Clipsham and T. Visser, Can. J. Chem., 42, 2754 (1964); (b) P.D. Bartlett and P. Günther, J. Amer. Chem. Soc., 88, 3288 (1966).

12. (a) E.M. Kosower, Accts. Chem. Res., 4, 193 (1971); (b) A.J.M. Jimenez, Diss. Abstr. Int. B., 31, 5878 (1971).

13. T. Imamoto, Bull. Chem. Soc. Japan, 45, 2216 (1972).

14. J.F. Bunnett and D.A.R. Happer, J. Org. Chem., 32, 2701 (1967).

15. L.A. Kazitsyna and N.B. Dzegilenko, Doklady Akad. Nauk SSSR, 192, 570 (1970).

16. H.V. Zwet and E.C. Kooyman, Rev. Trav. Chim., 86, 1143 (1967).

17. J.F. Bunnett and H. Takayama, J. Org. Chem., 33, 1924 (1968).

18. E.S Lewis, R.E. Holliday and L.D. Hartung, J. Amer. Chem. Soc., 91, 430 (1969).

19. D.F. McMillen, D.M. Golden and S.W. Benson, J. Amer. Chem. Soc., 94, 4403 (1972).

20. P. Knittel and J. Warkentin, Can. J. Chem., 53, 2275 (1975); Can. J. Chem., 54, 1341 (1976).

21. H.C. Ramsperger, J. Amer. Chem. Soc., 51, 2134 (1929).

22. (a) C.G. Overberger and J-P. Anselme, J. Amer. Chem. Soc., 86, 658 (1964); (b) C.G. Overberger, R.E. Zangora and J-P. Anselme, J. Org. Chem., 31, 2046 (1966); (c) C.G. Overberger, N. Weinshenker and J-P. Anselme, J. Amer. Chem. Soc., 87, 4119 (1965).

23. (a) D.E. McGreer, R.S. McDaniel and M.G. Vinje, Can. J. Chem., 43, 1389 (1965); (b) D.E. McGreer, N.W.K. Chiu, M.G. Vinje, Can. J. Chem., 43, 1398 (1965); (c) D.E. McGreer, N.W.K. Chiu, M.G. Vinje and K.C.K. Wong, Can. J. Chem., 43, 1407 (1965).

24. S. Seltzer and F.T. Dunne, J. Amer. Chem. Soc., 87, 2628 (1965).

25. W.A. Pryor and K. Smith, J. Amer. Chem. Soc., 92, 5403 (1970).

26. R.C. Neuman, Jr., and E.W. Ertley, J. Amer. Chem. Soc., 97, 3130 (1975).

27. K. Tagaki and R.J. Crawford, J. Amer. Chem. Soc., 93, 5910 (1971); 94, 7406 (1972).

28. (a) K.R. Kopecky and S. Evani, Can. J. Chem., 47, 4041 (1969), (b) K.R. Kopecky and J. Soler, Can. J. Chem., 52, 2111 (1974).

29. K. K-W. Shen and R.G. Bergman, J. Amer. Chem. Soc., 99, 1655 (1977).

30. N.A. Porter and L.J. Marnett, J. Amer. Chem. Soc., 95 4361 (1973).

31. H.J.H. Fenton, J. Chem. Soc., 65, 899 (1894).

32. C. Walling, Accts. Chem. Res., 8, 125 (1975).

33. J.H.P. Uttley, Ann. Reports B, 231 (1968), 217 (1969).

34. A. Carrington and A.D. McLachlan, Introduction to Magnetic Resonance, Harper and Row, New York, 1967.

35. R.W. Fessenden and R.H. Schuler, J. Chem. Phys., 39, 2147 (1963).

36. J.K. Kochi and P.J. Krusic, Essays in Free-Radical Chemistry, Chem. Soc. Special Publ., No. 24, (1970). p. 147.

37. R.O.C. Norman, Essays in Free-Radical Chemistry, Chem. Soc. Special Publ., No. 24, (1970). p. 117.

38. S. Forshult, C. Lagercrantz and K. Torsell, Acta. Chem. Scand., 23, 522 (1969).

39. C. Lagercrantz, J. Phys. Chem., 75, 3466 (1971).

40. I.H. Leaver, G.C. Ramsay and E. Suzuki, Aust. J. Chem., 22, 1891 (1969).

41. I.H. Leaver and G.C. Ramsay, Aust. J. Chem., 22, 1899 (1969).

42. A. Mack, Th.A.J.W. Wajer, Th.J. deBoer and J.D.W. van Voorst, Tet. Lett., 2155 (1966); 385 (1967).

43. E.G. Janzen, Accts. Chem. Res., 4, 31 (1971) and earlier work quoted there.

44. E.G. Rozantsec, Free Nitroxy Radicals, Plenum Press, New York, 1970.

45. A.R. Forrester, J.M. Hay and R.H. Thomson, Organic Chemistry of Stable Free Radicals, Academic Press, New York, 1968, p. 180.

46. A.L. Buchachenko, Stable Radicals, Consultants Bureau, New York, 1965.

47. E.G. Rozantsev and V.D. Sholle, Russ. Chem. Rev., 40, 233 (1971).

48. E.G. Rozantsev, Synthesis, 1, 190 (1971).

49. M.J. Perkins, Essays on Free Radical Chemistry, Chem. Soc. Spec. Publication, No. 24 (1970).

50. A. Rassat, Pure Appl. Chem., 25, 623 (1971).

51. E.G. Janzen and J.L. Gerlock, J. Amer. Chem. Soc., 91, 3108 (1969).

52. G.R. Chalfont and M.J. Perkins, J. Amer. Chem. Soc., 89, 3054 (1967).

53. C.M. Camaggi and M.J. Perkins, J. Chem. Soc. Perkin II, 507 (1972).

54. J.W. Hartgerink, J.B.F.N. Engberts, T.A.J.W. Wajer and Th.J. deBoer, Rec. Trav. Chim., Pays-Bas, 88, 481 (1969).

55. D.C. Gilbert, V. Malatesta and R.O.C. Norman, J. Amer. Chem. Soc., 93, 3290 (1971).

56. B.C. Gilbert, J.P. Larkin and R.O.C. Norman, J.C.S. Perkin II, 1272 (1972).

57. O.H. Griffith and A.S. Waggoner, Accts. Chem. Res., 2, 17 (1969).

58. C.L. Hamilton and H.M. McConnell, "Structural Chemistry and Molecular Biology", A. Rich and N. Davidson, Ed., W.H. Freeman and Co., Calif. (1968).

59. I.C.P. Smith, S.S. Muccillo and D. Marsh, Free Radicals in Biology, Vol. I, W.A. Pryor, Ed., Academic Press, New York (1976); Chapter 4.

60. C. Walling, Molecular Rearrangements, P. de Mayo, Ed., Interscience, New York (1963), Part 1, Chapter 7.

61. R.KH. Freidlina, Adv. Free-Radical Chem., 1 (1965). Chapter 6.

62. J.W. Wilt, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 8.

63. (a) H.E. Zimmerman and A. Zweig, J. Amer. Chem. Soc., 83, 1196 (1961).
    (b) N.F. Phelan, H.H. Jaffe and M. Orchin, J. Chem. Educ., 44, 626 (1967).

64. D.L. Struble, A.L.J. Beckwith and G.E. Gream, Tet. Lett., 3701 (1968).

65. M. Julia and M. Maumy, Bull. Soc. Chim. France, 2415, 2427 (1969) and earlier papers.

66. C. Walling and M.S. Pearson, J. Amer. Chem. Soc., 86, 2262 (1964).

67. T. Koenig and H. Fischer, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 4.

68. H.R. Ward, Accts. Chem. Res., 5, 18 (1972).

69. R.G. Lawler, Accts. Chem. Res., 5, 25 (1972).

70. R. Kaptein, Adv. Free Radical Chem., Vol. 5 (1975).

71. R.H. Ward, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 6.

72. R. Kaptein, J. Amer. Chem. Soc., 94, 6251, 6269 (1972).

73. P.D. Bartlett and T. Funahashi, J. Amer. Chem. Soc., 84, 2596 (1962).

74. K.U. Ingold and B.P. Roberts, Free-Radical Substitution Reactions, Interscience, New York (1971).

75. M.L. Poutsma, Free Radicals, J.K. Kochi, Ed., Vol. II, Wiley, New York (1973). Chapters 14 and 15.

59. I.C.P. Smith, S.S. Muccillo and D. Marsh, Free Radicals in Biology, Vol. I, W.A. Pryor, Ed., Academic Press, New York (1976), Chapter 4.

60. C. Walling, Molecular Rearrangements, P. de Mayo, Ed., Interscience, New York (1963), Part 1, Chapter 7.

61. R.Kh. Freidlina, Adv. Free-Radical Chem., 1 (1965). Chapter 6.

62. J.W. Wilt, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 8.

63. (a) H.E. Zimmerman and A. Zweig, J. Amer. Chem. Soc., 83, 1196 (1961).
(b) N.F. Phelan, H.H. Jaffe and M. Orchin, J. Chem. Educ., 44, 626 (1967).

64. D.L. Struble, A.L.J. Beckwith and G.E. Gream, Tet. Lett., 3701 (1968).

65. M. Julia and M. Maumy, Bull. Soc. Chim. France, 2415, 2427 (1969) and earlier papers.

66. C. Walling and M.S. Pearson, J. Amer. Chem. Soc., 86, 2262 (1964).

67. T. Koenig and H. Fischer, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 4.

68. H.R. Ward, Accts. Chem. Res., 5, 18 (1972).

69. R.G. Lawler, Accts. Chem. Res., 5, 25 (1972).

70. R. Kaptein, Adv. Free Radical Chem., Vol. 5 (1975).

71. R.H. Ward, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 6.

72. R. Kaptein, J. Amer. Chem. Soc., 94, 6251, 6269 (1972).

73. P.D. Bartlett and T. Funahashi, J. Amer. Chem. Soc., 84, 2596 (1962).

74. K.U. Ingold and B.P. Roberts, Free-Radical Substitution Reactions, Interscience, New York (1971).

75. M.L. Poutsma, Free Radicals, J.K. Kochi, Ed., Vol. II, Wiley, New York (1973). Chapters 14 and 15.

76. G.A. Russell, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 7.

77. R.S. Davidson, Quart. Rev., 21, 249 (1967).

78. A.L. William, E.A.Oberright and J.W. Brooks, J. Amer. Chem. Soc., 78, 1190 (1956).

79. M.S. Kharasch, J.L. Rowe and W.H. Urry, J. Org. Chem., 16, 905 (1951).

80. D.C. Neckers, A.P. Schaap and J. Hardy, J. Amer. Chem. Soc., 88, 1265 (1966).

81. D. Griller and K.U. Ingold, J. Amer. Chem. Soc., 96, 630 (1974).

82. I.H. Elson and J.K. Kochi, J. Org. Chem., 39, 2091 (1974).

83. L.J. Leyshon and D.H. Volman, J. Amer. Chem. Soc., 87, 5565 (1965).

84. A. Schönberg and A. Mustafa, J. Amer. Chem. Soc., 73, 2401 (1951).

85. B.R. Cowley and W.A. Waters, J. Chem. Soc., 128 (1961).

86. M. Nakasaki, J. Chem. Soc. Japan, 74, 405 (1953).

87. W.H. Urry, F.W. Stacey, O.O. Juveland and C.H. McDonnell, J. Amer. Chem. Soc., 75, 250 (1953); 76, 450 (1954).

88. C. Walling and E.S. Huyser, Org. React., 13, 109 (1963).

89. P. Gray, R. Shaw and J.C.J. Thynne, Progr. React. Kinet., 4, 65 (1967).

90. R.O.C. Norman, Chem. Soc. Special Publ., No. 24, 117 (1970).

91. J.F. Gibson, D.J.E. Ingram, M.C.R. Symons and M.G. Townsend, Trans. Faraday Soc., 53, 914 (1957).

92. M. Simonyi and F. Tüdös, Adv. Phys. Org. Chem., 9, 127 (1971).

93. F. Glockling, J. Chem. Soc., 3640 (1965).

94. (a) C.H. Depuy, G.M. Dappen and J.W. Hausser, J. Amer. Chem. Soc., 83, 3156 (1961).

94. (b) C.H. Depuy, H.L. Jones and D.H. Gibson, J. Amer. Chem. Soc., 90, 5306 (1968); 94, 3924 (1972).

95. R.S. Davidson, R.A. Sheldon and S. Trippett, J. Chem. Soc. (C), 7222 (1966); Chem. Comm. 99 (1966).

96. P. Gray and A.A. Herod, Trans. Faraday Soc., 64, 1568 (1968).

97. V.B. Koutecky, J. Koutecky and L. Salem, J. Amer. Chem. Soc., 99, 842 (1977).

98. J.E. Bloor, A.C.R. Brown and D.G.L. James, J. Phys. Chem., 70, 2191 (1966) and their earlier papers.

99. J.M. Tedder and J.C. Walton, Accts. Chem. Res., 9, 183 (1976).

100. G. Sosnovsky, Free Radical Reactions in Preparative Organic Chemistry, Macmillan, London, 1964.

101. C. Walling and E.S. Huyser, Org. React., 13, 91 (1963).

102. F.W. Stacey and J.F. Harris, Org. React., 13, 150 (1963).

103. P.I. Abell, Free Radicals, J.K. Kochi, Ed., Vol. II, Wiley, New York (1973), Chapter 13.

104. F. Minisci, Accts. Chem. Res., 8, 165 (1975).

105. R.S. Neale, Synthesis, 1, 1 (1971).

106. K. Griesbaum, Angew. Chem. Int. Ed., 9, 273 (1970).

107. B. Vollmert, Polymer Chemistry, Springer-Verlag, New York (1973).

108. F.R. Mayo, J. Amer. Chem. Soc., 84, 3964 (1962).

109. J.M. Tedder, Prog. Chem. Soc., 80 (1961).

110. H.W. Sidebottom, J.M. Tedder and J.C. Walton, Trans. Faraday Soc., 65, 2103 (1969).

111. E.S. Huyser and R.M. Kellogg, J. Org. Chem., 30, 2867 (1967).

112. K. Griesbaum, Angew. Chem. Int. Ed., 9, 273 (1970).

113. R.A. Jackson, Adv. Free-Radical Chem., 3, 231 (1969).

114. N.T. Friswell and B.G. Gowenlock, Adv. Free-Radical Chem., 1, 39 (1965).

115. P.S. Skell and R.G. Allen, J. Amer. Chem. Soc., 80, 5997 (1958); 79, 1253 (1957); 81, 5383 (1959).

116. H.L. Goering and D.W. Larsen, J. Amer. Chem. Soc., 81, 5937 (1959).

117. F.W. Stacey and J.F. Harris, Org. React., 13, 150 (1963), p. 157.

118. J. Weinstock, Am. Chem. Soc. Meeting Abstr., 128, 19-0 (1955).

119. S.J. Cristol, R.P. Arganbright, G.D. Brindell and R.M. Heintz, J. Amer. Chem. Soc., 179, 6039 (1957).

120. R. Gregory, R.N. Haszeldine and A.E. Tipping, J. Chem. Soc. (C), 1750 (1970).

121. D.P. Johari, H.W. Sidebottom, J.M. Tedder and J.C. Walton, J. Chem. Soc. (B), 95 (1971).

122. J.I.G. Cadogan and D.H. Hey, Quart. Rev., 8, 308 (1954).

123. R.L. Huang, J. Chem. Soc., 1749 (1956); 1342 (1957).

124. J.M. Tedder and J.C. Walton, Prog. React. Kinetics, 4, 39 (1967).

125. J.A. Kerr and M.J. Parsonage, "Evaluated Kinetic Data on Gas Phase Addition Reactions", Butterworths, London (1972).

126. D.H. Hey, J.I.G. Cadogan and S.H. Ong, J. Chem. Soc., 1939 (1965).

127. R.L. Juang, H.H. Lee and L.Y. Wong, J. Chem. Soc., 6730 (1965).

128. G.I. Nikishin, V.D. Vorob'ev, A.D. Petrov, Doklady Akad. Nauk SSSR, 136, 360 (1961); and Reference 87.

129. M.S. Kharasch, M. Zimmerman, W. Zimmt and W. Nudenberg, J. Org. Chem., 18, 1045 (1953).

130. J.K.S. Wan, L.D. Hess and J.[illegible]. Pitts, J. Amer. Chem. Soc., 86, 2069 (1964).

131. V. Malatesta and K.U. Ingold, Te[illegible]Lett., 3307 (1973).

132. G.O. Pritchard, H.O. Pritchard and A.F. Trotman-Dickenson, Chem. and Ind., 564 (1955).

133. G.O. Pritchard, H.O. Pritchard, H.I. Schiff and A.F. Trotman-Dickenson, Trans. Faraday Soc., 52, 849 (1956).

134. V. Rehak, F. Novak, J. Kuncicky and I. Cepeiansky, Tetrahedron Lett., 23, 1967 (1970).

135. J.L. Kice and R.S. Gabrielsen, J. Org. Chem., 35, 1004, 1010 (1970).

136. H. Lui and J. Warkentin, Can. J. Chem., 51, 1148 (1973).

137. J.K. Kochi, Science, 155, 415 (1967).

138. F. Basolo and R.G. Pearson, Mechanisms of Inorganic Reactions, Wiley, New York (1967), p. 454.

139. J.S. Littler, Free Radical Reactions, W.A. Waters, Ed., MTP Int. Rev. of Science, Organic Chem. Series One, Vol. 10, Butterworths, London (1973).

140. J.K. Kochi, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973), Chapter 11.

141. J.F. Garst, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973), Chapter 9.

142. J.H. Raley, F.F. Rust and W.E. Vaughan, J. Amer. Chem. Soc., 70, 1336 (1948).

143. E.S. Huyser and R.M. Van Scoy, J. Org. Chem., 33, 3524 (1968).

144. C. Walling and B. Miller, J. Amer. Chem. Soc., 79, 4181 (1957).

145. A.A. Zavitsas and J.A. Pinto, J. Amer. Chem. Soc., 94, 7390 (1972).

146. S.F. Nelsen, Free Radicals, J.K. Kochi, Ed., Vol. II, Wiley, New York (1973), Chapter 21.

147. A. Ohno and Y. Ohnishi, Tet. Lett., 50, 4405 (1969).

148. G.A. Russell, J. Amer. Chem. Soc., 79, 2977 (1957); 80, 4987 (1958).

149. R.H. Huang, T.W. Lee and S.H. Ong, J. Chem. Soc. (C), 40 (1969).

150. Yu. L. Spirin, Russ. Chem. Rev., 38, 529 (1969).

151. E.S. Huyser, Adv. Free-Radical Chem., 1 (1965), Chapter 3.

152. J.C. Martin, Free Radicals, J.K. Kochi, Ed., Vol. II, Wiley, New York (1973). Chapter 20.

153. J.A. Kerr, Chem. Rev., 66, 465 (1966).

154. S.W. Benson, J. Chem. Educ., 42, 502 (1965).

155. H.E. O'Neal and S.W. Benson, Free Radicals, J.K. Kochi, Ed., Vol. II, Wiley, New York (1973). Chapter 17.

156. E.F.P. Harris and W.A. Waters, Nature, 170, 211 (1952).

157. K.E.J. Barrett and W.A. Waters, Discuss. Faraday Soc., 14, 221 (1953).

158. R.M. Kellogg, in "Methods in Free Radical Chemistry", (E.S. Huyser, Ed.), Vol. 2, p. 1, Dekker, New York (1969).

159. S.G. Cohen and C.H. Wang, J. Amer. Chem. Soc., 77, 4435 (1955); 79, 1924 (1957).

160. P.S. Skell and R.G. Allen, J. Amer. Chem. Soc., 82, 1511 (1960).

161. E.S. Huyser and R.M.Kellogg, J. Org. Chem., 31, 3366 (1966).

162. J.K. Kochi, Free Radicals, J.K. Kochi, Ed., Vol. I, Wiley, New York (1973). Chapter 11, p. 627.

163. J.K. Kochi, Accts. Chem. Res., 7, 351 (1974).

164. The first application of LTA was reported in 1923. O. Dirmorth and R. Schweizer, Ber., 56B, 1375 (1923).

165. R. Criegee and C.A. Bunton,"Oxidation in Organic Chemistry", K.B. Wiberg, Ed., Academic Press, New York (1965). p. 398.

166. R.S. Perlin, Adv. Carbohyd. Chem., 14, 9 (1959).

167. K. Hensler and J. Kalvoda, Angew. Chem. Int. Ed., 3, 525 (1964).

168. R.N. Butler, Chem. Ind. (London), 523 (1972).

169. S. Forshult, C. Lagercrantz and K. Torssell, Acta. Chem. Scand., 23, 522 (1969).

170. P.R. West, Ph.D. Thesis, McMaster University (1967).

171. P. Knittel, Ph.D. Thesis, McMaster University (1975).

172. R.N. Butler, Chem. Ind. (London), 437 (1968).

173. R.N. Butler, F.L. Scott and T.A.F. O'Mahony, Chem. Rev., 73, 93 (1973).

174. B.T. Gillis and M.P. LaMontagne, J. Org. Chem., 32, 3318 (1967); 33, 762, 1294 (1968).

175. J.B. Aylward, Quart. Rev. Chem. Soc., 25, 407 (1971).

176. J. Warkentin, Synthesis, 279 (1970).

177. D.H.R. Barton, J.F. McGhie and P.L. Batter, J. Chem. Soc. C, 1033 (1970).

178. A. Stojiljkovic, N. Orbovic, S. Sredojevic and M.Lj. Mihailovic, Tetrahedron, 26, 1101 (1970).

179. D.M. Gale, W.J. Middleton and C.G. Krespan, J. Amer. Chem. Soc., 88, 3617 (1966).

180. J. Jacques, C. Wiedmann and A. Horeau, Bull. Soc. Chim. France, 424 (1959).

181. E. Ciganek, J. Amer. Chem. Soc., 87, 657 (1965).

182. E. Ciganek, J. Org. Chem., 30, 4198 (1965); 35, 862 (1970).

183. M. Debono and R.M. Molloy, J. Org. Chem., 34, 1454 (1969).

184. D.C. Iffland, L. Salisbury and W.R. Schafer, J. Amer. Chem. Soc., 83, 747 (1961).

185. B.C. Gilbert and R.O.C. Norman, J. Chem. Soc. B, 86 (1966) and other papers in the series.

186. M.J. Harrison, R.O.C. Norman and W.A.F. Gladstone, J. Chem. Soc. C, 735 (1967).

187. J. Bornstein and L. Skarlos, J. Org. Chem., 35, 1230 (1970).

188. B.T. Gillis and K.F. Schimmel, J. Org. Chem., 32, 2865 (1967).

189. W.A.F. Gladstone and R.O.C. Norman, J. Chem. Soc. C, 1531 (1966), and other papers in the series.

190. A. Bhati, Chem. Comm., 476 (1965).

191. J. Buckingham and R.D. Guthrie, J. Chem. Soc. C, 1445 (1968).

192. G.B. Gubelt and J. Warkentin, Can. J. Chem., 47, 3983 (1969).

193. R. Kuhn and W. Murrzing, Chem. Ber., 85, 29 (1952).

194. J.P. Freeman, J. Org. Chem., 28, 885 (1963); 29, 1379 (1964).

195. W.A.F. Gladstone and R.O.C. Norman, J. Chem. Soc. C, 5177 (1965).

196. A. Bhati, J. Chem. Soc., 1020 (1965).

197. N. Rabjohn and M.C. Chaco, J. Org. Chem., 30, 3227 (1965).

198. R.W. Hoffmann and H.L. Luthardt, Tetrahedron Lett., 411 (1966).

199. R.W. Hoffmann and H.L. Luthardt, Tetrahedron Lett., 3501 (1967).

200. R.W. Hoffmann and H.L. Luthardt, Chem. Ber., 101, 3851 (1968).

201. R.W. Hoffmann and H.L. Luthardt, Chem. Ber., 101, 3861 (1968).

202. D.C. Iffland and E. Cerda, J. Org. Chem., 28, 2769 (1963).

203. E. Schmitz, R. Ohme and S. Schramm, Angew. Chem. Int. Ed. Engl., 2, 157 (1963).

204. E. Schmitz, R. Ohme and S. Schramm, Ann. Chem., 702, 131 (1967).

205. S. Hünig and J. Cramer, Angew. Chem. Int. Ed. Engl., 7, 943 (1968).

206. S. Hünig and G. Büttner, Angew. Chem. Int. Ed. Engl., 8, 451 (1969).

207. G. Büttner and S. Hünig, Chem. Ber., 104, 1088, 1104 (1971).

208. G. Büttner, J. Cramer, L. Geldern and S. Hünig, Chem. Ber., 104, 1118 (1971).

209. R. Allmann and I. Kawada, Angew. Chem. Int. Ed. Engl., 7, 944 (1968).

210. J.P. Freeman and C.P. Rathjen, Chem. Comm., 538 (1969).

211. J.P. Freeman and C.P. Rathjen, J. Org. Chem., 37, 1686 (1972).

212. R.C. Jain and J. Warkentin, unpublished results in this laboratory (1975).

213. P.L. Southwick, N. Latif, J.E. Klijanowicz and J.G. O'Connor, Tet. Lett., 1767 (1970).

214. R.J. Crawford, A. Mishra and R. Dummel, J. Amer. Chem. Soc., 88, 3959 (1966).

215. W. Nagata and S. Kamata, J. Chem. Soc. C, 540 (1970).

216. R. Stollé and J. Laux, Chem. Ber., 44, 1127 (1911).

217. A. Schönberg and M.Z. Barakat, Chem. Ber., 71B, 995 (1938).

218. K.V. Anwers and H. Wunderling, Chem. Ber., 68, 1072 (1935).

219. (a) W.H. Hunter and W.S. Dyer, J. Amer. Chem. Soc., 55, 5053 (1933).
(b) W.M. Lauer and W.S. Dyer, J. Amer. Chem. Soc., 64, 1453 (1942).

220. A. Schönberg and M.Z. Barakat, J. Chem. Soc., 1074 (1939).

221. W. Kirmse, Chem. Ber., 93, 2357 (1960).

222. C.J. Michejda, Tetrahedron Lett., 2281 (1968).

223. N.P. Gambaryan, L.A. Simonyan and I.L. Knunyants, Doklady Akad. Nauk SSSR, 155, 833 (1964).

224. P. Rajagopalan and B.G. Advani, Tetrahedron Lett., 2689 (1967).

225. P.R. West and J. Warkentin, J. Org. Chem., 34, 3233 (1969).

226. P.C. Ip, K. Ramakrishnan and J. Warkentin, Can. J. Chem., 52, 3671 (1974).

227. K. Ramakrishnan, J.B. Fulton and J. Warkentin, Tetrahedron, 32, 2685 (1976).

228. K. Ramakrishnan, Ph.D. Thesis, McMaster University (1975).

229. S.L. Lee, A.M. Cameron and J. Warkentin, Can. J. Chem., 50, 2326 (1972).

230. G.H. Coleman, H. Gilman, C.E. Adams and P.E. Pratt, J. Org. Chem. 3, 99 (1938).

231. R. Huisgen, Angew. Chem. 67, 439 (1955).

232. P.A.S. Smith, J.M. Clegg and J. Lakirtz, J. Org. Chem. 23, 1595 (1958).

233. S.G. Cohen and C.H. Wang, J. Amer. Chem. Soc. 77, 3628 (1955).

234. A.F. Hegarty and F.L. Scott, J. Chem. Soc. (B), 1031 (1966).

235. D.S. Malament, Ph.D. Thesis, Yale University, 1970.

236. I.H Leaver and G.C. Ramsay, Tetrahedron, 25, 5669 (1969).

237. E.H. Man, F.C. Frostick, Jr. and C.R. Hauser, J. Amer. Chem. Soc. 74, 3230 (1952).

238. S.H. Powell and W.J. Wasserman, J. Amer. Chem. Soc. 79, 1937 (1957).

239. J.E. Mulvaney and Z.G. Garlund, J. Org. Chem. 30, 917 (1965).

240. Sadtler Standard Spectra, NMR # 5997; IR # 17523.

241. Ming-Chien Chiang (Natl. Univ. - Peking), J. Chinese Chem. Soc. 18, 65 (1951).

242. E.I. Klimova, E.G. Treshchova and Yu. A. Arbuzov, Dokl. Akad. Nauk SSSR 180, 865 (1968)

243. Sadtler Standard Spectra, NMR # 3696, IR # 20785.

244. H. Brunner and E.H. Farmer, J. Chem. Soc. 1039 (1937).

245. Sadtler Standard Spectra, IR # 31896.

246. Sadtler Standard Spectra, NMR # 8096; IR # 24944.

247. Sadtler Standard Spectra, NMR # 33; IR # 261.

248. Sadtler Standard Spectra, NMR # 6787; IR # 5250.

249. J.B. Stothers, C.T. Tan, and K.C. Teo, Can. J. Chem. 51, 2893 (1973).

250. J.W.B. Reesor and G.F. Wright, J. Org. Chem. 22, 375 (1957).

251. K. Berg-Nielsen and E. Bernatek, Acta. Chem. Scand. 26, 4130 (1972).

252. P.F. Holt and B.P. Hughes, J. Chem. Soc. 764 (1954).

253. D.J. Cram, J.B. Hendrickson and G.S. Hammond, Organic Chemistry, 3rd Ed., McGraw-Hill, N.Y., 1971.

254. D.E. Williams, J. Amer. Chem. Soc. 89, 4280 (1967).

255. The value is taken from the CRC Handbook of Chemistry and Physics, 52nd Ed., 1971-72.

256. L.A. Kalashnikova, A.L. Buchachenko, M.B. Neiman and E.G. Rosantsev, Zhur. Fiz. Khim. 43, 64 (1969).

257. V. Malatesta and K.U. Ingold, Tetrahedron Lett., 3307 (1973).

258. K. Biemann, Mass Spectrometry: Organic Chemical Applications, McGraw-Hill, New York, 1962.

259. The ^{2}Hmr spectrum was obtained by Dr. J.B. Stothers at the University of Western Ontario, London, Ontario.

260. G. Chapelet-Letournexux, H. Lemaire, and A. Rassat, Bull. Soc. Chim. France, 3283 (1965).

261. J.C. Baird and J.R. Thomas, J. Chem. Phys. 35, 1507 (1961).

262. H. Lemaire and A. Rassat, J. Chim. Phys. 61, 1580 (1964).

263. H. Lemaire, Y. Marechal, R. Ramasseul and A. Rassat, Bull. Soc. Chim. France, 372 (1965).

264. C. Chachaty and A. Forchioni, Tetrahedron Lett. 3, 307 (1968).

265. B.C. Gilbert, R.O.C. Norman and D.C. Price, Prog. Chem. Soc. 234 (1964), and other papers in the series.

266. R.A. Turner, J. Amer. Chem. Soc. 69, 877 (1947).

267. R.H. McGirk, C.R. Cyr, W.D. Ellis and E.H. White, J. Org. Chem. 39 3351 (1974).

268. E.D. Becker, High Resolution NMR Theory and Chemical Applications, Academic Press, New York, 1969.

269. D.C. Iffland and L.M. Weisenberger, paper presented at the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept., 1967.

270. C.G. Pitt, J. Org. Chem. 30, 3242 (1965).

271. Sadtler Standard Spectra, NMR # 179289; IR # 44931.

272. Personal communication from Dr S.C. Wicherink, Catholic University, Nijmegen, The Netherlands.

273. C. Rückardt, Angew. Chem. Int. Ed. 4, 29 (1965).

274. P.D. Gardner, J. Amer. Chem. Soc. 78, 3421 (1956).

275. H.J. Shine and G.E. Hunt, J. Amer. Chem. Soc. 80, 2434 (1958).

276. N.J. Turro and P.A. Wriede, J. Amer. Chem. Soc. 90, 6863 (1968); 92, 320 (1970).

277. N.J. Turro and P.A. Wriede, J. Org. Chem. 34, 3562 (1969).

278 L.I. Smith and K.L. Howard, Org. Syn. Coll. Vol. 3, 352 (1955).

279. J.B. Miller, J. Org. Chem. 24, 560 (1959).

280. W. Schroeder and L. Katz, J. Org. Chem. 19, 718 (1954).

281. L. Fieser and M. Fieser, Reagents for Organic Synthesis, John Wiley and Sons, New York, N.Y., 1967, page 537.

282. A.I. Vogel, Qualitative Organic Analysis, Part 2, 2nd Ed., ELBS and Longman, London, 1971, page 354.

283. J. Warkentin and K.E. Hine, Can. J. Chem. 48, 3545 (1970).

284. J. Warkentin, J. Chem. Educ. 43, 265 (1966).

285. P.F. Holt and B.P. Hughes, J. Chem. Soc., 764 (1954).

286. M.M. Movsumzade and N.G. Abdullaev, Azerb. Khim. Zh., p. 45 (1966).

287. W.B. Smith and T.K. Chen, J. Org. Chem. 30, 3095 (1965).

288. S. Moon and H. Bohm, J. Org. Chem. 37, 4338 (1972).

APPENDIX I

A COMPUTER PROGRAM FOR EVALUATING FIRST-ORDER RATE CONSTANTS

```
      PROGRAM MAIN(INPUT, OUTPUT, TAPE 5=INPUT)
      DIMENSION X(50), Y(50), A(5), B(2), YTHEO(50), LABEL(8), YDEVIA(5
     10), C(50), CPREL(50), BSLOPE(50), W(50), S(7)
C     FIT THE DATA X(I) AND Y(I) INTO A EQUATION OF Y(I)=B(1)+B(2)*X(I)
    1 READ 101, LABEL
  101 FORMAT (8A10)
      IF (EOF(5)) 999, 2
    2 READ 102, N
  102 FORMAT (I2)
      M=1
      READ 103, (X(I), I=1,N)
  103 FORMAT (8F10.5)
      READ 103, (C(I),I=1,N)
      DO 1000 I=1,N
      CPREL(I)=C(1)/C(I)
      Y(I)=ALOG(CPREL(I))
 1000 CONTINUE
      TG=0.
      DO 4 I=1,N
      W(I)=CPREL(I)**2
      TG=TG+W(I)
    4 S(I)=0.
      TG=TG/N
      DO 5 I=1,N
      W(I)=W(I)/TG
      S(5)=S(5)+Y(I)**2*W(I)
      S(3)=S(3)+Y(I)*W(I)
      S(1)=S(1)+X(I)*W(I)
      S(2)=S(2)+X(I)**2*W(I)
    5 S(4)=S(4)+X(I)*Y(I)*W(I)
      B(2)=(N*S(4)-S(1)*S(3))/(N*S(2)-S(1)**2)
      B(1)=(S(3)-B(2)*S(1))/N
      S(6)=S(5)-(S(3)**2)/N
      S(7)=(B(2)**2)*(S(2)-(S(1)**2)/N)
      REG=S(7)/S(6)
      R=SQRT((S(6)-S(7))/(N-2))
      BSTD=SQRT(S(2)/(N*(S(2)-(S(1)**2/N))))*R
      SSTD=R/SQRT(S(2)-(S(1)**2/N))
      DO 3 I=1,N
      YTHEO(I)=B(1)+B(2)*X(I)
      YDEVIA(I)=YTHEO(I)-Y(I)
      IF(I.EQ.1) BSLOPE(1)=0.
      IF(I.NE.1) BSLOPE(I)=B(2)-Y(I)/X(I)
    3 CONTINUE
      PRINT 104, LABEL
  104 FORMAT(1H1,8A10)
      PRINT 105, N
  105 FORMAT (///,10X,*NO.OF POINTS IS*, I3)
      PRINT 106, (X(I),I=1,N)
  106 FORMAT (///,10X,*THE INPUT TIME ARE *,/,12F10.5)
      PRINT 107, (C(I), I=1,N)
  107 FORMAT (///,10X,* THE INPUT C ARE *,/,12F10.5)
      PRINT 120, (Y(I),I=1,N)
  120 FORMAT (///,10X,* THE LOGC ARE *,/, 12F10.5)
      PRINT 108, B(1), B(2)
  108 FORMAT (///,10X,* THE LEAST SQUARE EQUATION IS *,5X,*LOGC(I)=*,F1
     1.6, *+*, F10.5, 5H*T(I))

      PRINT 109, (YTHEO(I), I=1,N)
  109 FORMAT (///,10X,* THE CALCULATED Y ARE *,/,12F10.5)
      PRINT 110, (YDEVIA(I), I=1,N)
  110 FORMAT (///,10X,* THE DEVIATION IN Y ARE *, /, 12F10.5)
      PRINT 130, (BSLOPE(I),I=1,N)
  130 FORMAT (///,10X,*  THE DEVIATION IN SLOPE ARE *,/,12F10.5)
      PRINT 111, B(2), SSTD, REG
  111 FORMAT (///,10X, * THE SLOPE IS *, F10.6, *WITH STD DEV*, F15.10,
     110X, * CORRELATION COEFFICIENT *, F8.6)
      GO TO 1
  999 CALL EXIT
      END
```